

HEART.

A JOURNAL FOR THE STUDY OF THE CIRCULATION.

EDITED BY
THOMAS LEWIS, M.D.,

AIDED IN THE SELECTION OF PAPERS BY

Dr. W. H. GASKELL.

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STATEMENT

IN TESTIMONY WHEREOF, THE SIGNED AND SEALED
THIS 10th DAY OF APRIL 1968

AT WASHINGTON, D.C.

THE PRESIDENT OF THE UNITED STATES OF AMERICA

JOHN F. KENNEDY
President of the United States of America

JOHN F. KENNEDY



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ERRATA.

- Page 4. Four lines from bottom. "Cash and Dunstan mention that the auricle often beats in 1:2 rhythm," etc., *to read* "Cash and Dunstan suggest the possibility of reversion occurring under aconitine in reference to another form of irregularity observed by them."
- Page 22. Reference 11. "Hoffmann" *to read* "Hofmann"; insert page 130.
Reference 14. "1907, IV, 1," *to read* "1907, IV, 681."
- Page 38. Headline. "NODAL RHYTHM" *to read* "NODAL BRADYCARDIA."
- Page 42. Lines 1 and 2. "cava wall, of the right auricle and" *to read* "cava wall of the right auricle, and"
- Page 116. Headline. "ALTERNATION OF THE AURICLE" *to read* "ALTERNATION."
- Page 138. Line 2. "alterative" *to read* "alternative."
- Page 166. Reference 22. "Therap. Gazette" *to read* "ibid."
- Page 252. Four lines from bottom. "later development of the base" *to read* "later developed base."

CONTENTS OF VOL. I.

No. 1. (*Issued July 1, 1909.*)

| | PAGE |
|--|------|
| PREFATORY NOTE. By W. H. Gaskell | v. |
| EDITORIAL PREFACE | vii. |
| THE IRREGULARITIES OF THE MAMMALIAN HEART OBSERVED UNDER ACONITINE AND ON ELECTRICAL STIMULATION. By Arthur R. Cushny. (<i>From the Pharmacological Laboratory, University College, London</i>) | 1 |
| NODAL BRADYCARDIA. By James Mackenzie | 23 |
| PAROXYSMAL TACHYCARDIA. By Thomas Lewis. (<i>University College, London</i>) | 43 |
| THE MEASUREMENT OF SYSTOLIC BLOOD PRESSURE IN MAN. By Leonard Hill. <i>With the co-operation of Mr. Martin Flack and Dr. W. Holtzmann. (From the Physiological Laboratory, London Hospital Medical School)</i> .. | 73 |

No. 2. (*Issued November 1, 1909.*)

| | |
|---|-----|
| THE REGULAR OCCURRENCE OF INTERPOLATED EXTRASYSTOLES. By E. E. Laslett. (<i>Hull.</i>) | 83 |
| THE RATE OF BLOOD FLOW IN THE ARM. By A. W. Hewlett and J. G. Van Zwaluwenburg. (<i>Department of Internal Medicine, University of Michigan</i>) | 87 |
| THE EXPERIMENTAL PRODUCTION OF PAROXYSMAL TACHYCARDIA AND THE EFFECTS OF LIGATION OF THE CORONARY ARTERIES. By Thomas Lewis. (<i>From the Research Laboratories, University College Hospital Medical School. (Dr. Charles Bolton.)</i>) | 98 |
| THE ACTION OF AN ACTIVE PRINCIPLE FROM APOCYNUM. By H. H. Dale and P. P. Laidlaw. (<i>From the Physiological Laboratory, Guy's Hospital, and the Wellcome Physiological Research Laboratories, Home Hall, S.E.1.</i>) | 138 |
| ON THE AURICULO-NODAL JUNCTION. By Alfred E. Cohn. (<i>New York.</i>) .. | 167 |

CONTENTS

No. 3. (Issued January 1, 1910.)

| | PAGE |
|---|------|
| FURTHER STUDIES IN THE PHYSIOLOGY OF HEART-BLOCK IN MAMMALS. CHRONIC AURICULO-VENTRICULAR HEART-BLOCK IN THE DOG. By Joseph Erlanger and Julian R. Blackman. (<i>With histological reports by E. K. Cullen and W. S. Miller.</i>) (<i>From the Physiological Laboratories of the Johns Hopkins University, and of the University of Wisconsin</i>) .. | 177 |
| BREAST PANG. By H. Walter Verdon. (<i>London.</i>) | 230 |
| THE SUCCESSION OF EVENTS IN THE CONTRACTING VENTRICLE AS SHOWN BY ELECTROMETER RECORDS—(TORTOISE AND RABBIT). By Francis Gotch. (<i>Physiological Laboratory, Oxford.</i>) | 235 |
| PAROXYSMAL TACHYCARDIA, THE RESULT OF ECTOPIC IMPULSE FORMATION. By Thomas Lewis. (<i>University College, London.</i>) | 262 |

No. 4. (Issued March 30, 1910.)

| | |
|--|-----|
| INDEPENDENT VENTRICULAR RHYTHM: HEART-BLOCK AND THE STOKES- ADAMS SYNDROME WITHOUT AFFECTION OF CONDUCTIVITY. By A. M. Gossage. (<i>Westminster Hospital, London.</i>) | 283 |
| NOTE ON THE BLOOD-PRESSURE AND LYMPH FLOW IN A CASE OF HEART DISEASE IN A DOG. By C. Bolton and E. H. Starling. (<i>From the Institute of Physiology, University College.</i>) | 292 |
| SINUS ARRHYTHMIA, ASSOCIATED WITH ANGINAL ATTACKS OF A VASO-MOTOR TYPE. By Kenneth H. Stokes. (<i>University College Hospital, London.</i>) | 297 |
| AURICULAR FIBRILLATION AND ITS RELATIONSHIP TO CLINICAL IRREGULARITY OF THE HEART. By Thomas Lewis. (<i>From the Research Laboratories University College Hospital Medical School.</i>) | 306 |

LIST OF AUTHORS.

| | PAGE |
|---|------|
| BLACKMAN, JULIAN R., and ERLANGER, JOSEPH. "Further Studies in the Physiology of Heart-Block in Mammals. Chronic Auriculo-Ventricular Heart-Block in the Dog" | 177 |
| BOLTON, C., and STARLING, E. H. "Note on the Blood Pressure and Lymph Flow in a Case of Heart Disease in a Dog" | 292 |
| COHN, ALFRED E. "On the Auriculo-Nodal Junction" | 167 |
| CUSHNY, ARTHUR R. "The Irregularities of the Mammalian Heart observed under Aconitine and on Electrical Stimulation" | 1 |
| DALE, H. H., and LAIDLAW, P. P. "The Action of an Active Principle from Apocynum" | 138 |
| ERLANGER, JOSEPH, and BLACKMAN, JULIAN R. "Further Studies in the Physiology of Heart-Block in Mammals. Chronic Auriculo-Ventricular Heart-Block in the Dog" | 177 |
| GASKELL, W. H. Prefatory Note | v. |
| GOSSAGE, A. M. "Independent Ventricular Rhythm: Heart-Block and the Stokes-Adams Syndrome without Affection of Conductivity" | 283 |
| GOTCH, FRANCIS. "The Succession of Events in the Contracting Ventricle as shown by Electrometer Records—(Tortoise and Rabbit)" | 235 |
| HEWLETT, A. W., and VAN ZWALUWENBURG, J. G. "The Rate of Blood Flow in the Arm" | 87 |
| HILL, LEONARD. "The Measurement of Systolic Blood Pressure in Man" | 73 |
| LAIDLAW, P. P., and DALE, H. H. "The Action of an Active Principle from Apocynum" | 138 |
| LASLETT, E. E. "The Regular Occurrence of Interpolated Extrasystoles" | 83 |
| LEWIS, THOMAS. "Paroxysmal Tachycardia" | 43 |
| "The Experimental Production of Paroxysmal Tachycardia and the Effects of Ligation of the Coronary Arteries" | 98 |
| "Paroxysmal Tachycardia, the Result of Ectopic Impulse Formation" | 262 |
| "Auricular Fibrillation and its Relationship to Clinical Irregularity of the Heart" | 306 |
| MACKENZIE, JAMES. "Nodal Bradycardia" | 23 |

LIST OF AUTHORS

| | PAGE |
|---|------|
| STARLING, E. H., and BOLTON, C. "Note on the Blood-Pressure and Lymph Flow in a Case of Heart Disease in a Dog" | 292 |
| STOKES, KENNETH H. "Sinus Arrhythmia, associated with Anginal Attacks of a Vaso-Motor Type" | 297 |
| VAN ZWAMENBURG, J. G., and HEWLETT, A. W. "The Rate of Blood Flow in the Arm" | 87 |
| VERDON, H. Walter. "Breast Paug" | 230 |

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PREFATORY NOTE.

YEAR by year as the Twentieth Century rolls on it becomes evident that the experimental sciences of Physiology, Pathology, and Pharmacology are more and more directly influencing the study and practice of medicine. Slowly but surely the methods which have proved of value in the laboratory are becoming a matter of routine practice in the hospital for purposes of diagnosis ; slowly but surely the results of experiments gained in the laboratories are being applied to man. Medical study is losing its empiric character, and is founding itself on the well ascertained facts of Physiology and its cognate sciences, Pathology and Pharmacology. More and more, then, is it of vital importance for the medical man to keep in touch with the workers in the laboratories, and to apply the most recent knowledge gained by them directly to man.

In all such problems as those connected with sensations of different kinds it is clear that we have to rely directly upon clinical observation.

It is, therefore, most advisable for further progress that each of these two classes of investigators should be enabled to ascertain what the other is doing in the easiest possible way. In the case of the nervous system the end required has been accomplished by the formation of the Neurological Society, and the publication of the journal "Brain."

It is felt by an increasing number of workers especially interested in the investigation of problems connected with the heart and circulatory system that the time has come for the publication of a journal devoted entirely to these subjects.

The book on the Heart recently published by Mackenzie has aroused the interest of medical men by showing the importance of accurately studying by the graphic method the condition of the heart and circulation in man himself, and how by the aid of the knowledge obtained in the laboratories curves so obtained may be interpreted. Recent invention and observation have opened up a wide field for further investigation of the fluctuations of arterial blood pressure, which occur in man, and their relation to health and disease.

The Journal will be of great value to the medical man, as it will focus together the work of the laboratory and the work of the hospital ward, and to the physiologist, because during his investigations it will keep ever present to his mind the nature of the problems which, in the opinion of the medical man, are pressing urgently for solution. Such a co-operation between those interested in the physiological and clinical aspects of the problems connected with the circulation, as is implied in the starting of the Journal, will, I feel sure, be so heartily welcomed amongst English-speaking nations, as to ensure the success of the Journal.

W. H. GASKELL.

EDITORIAL PREFACE.

IT has been decided that it is now essential that those specially seeking new facts and new conclusions relating to hæmodynamic problems should reap the advantages of a special Journal, in which such facts and the conclusions drawn from them may be placed on record.

This resolve comes from the conviction that students of the circulation are now seriously hampered in their work by the difficulty of keeping in touch with the papers that appear, so widely scattered, in the various publications of more general scope.

The Journal affirms a single object, the progress of knowledge of the mechanism by which the blood circulates in health and disease. A closer union of thought amongst workers in the separate branches of medical science must contribute to the attainment of this end.

To know the pump, which Harvey revealed to us, more intimately ; to understand more definitely the forces which regulate its action, and the mechanism by which it distributes the constant stream of blood, bathing and feeding the tissues of the body : to determine the causes which impair the circulatory functions : to see more clearly the means of prevention and the remedies which palliate where injury to the heart or vessels is concerned : such is the scope of this Journal. The field is sufficient for many workers.

The Journal requires communications, containing, above all, original and carefully ascertained facts, and conclusions consonant with such facts and previous observations. By a record of fact and the statement of new principles progress will be ensured.

The advances of recent years are largely indebted to Gaskell and his work for their initiation, and this Journal heartily appreciates the message he sends it as it takes the first step on its course.

THE IRREGULARITIES OF THE MAMMALIAN HEART OBSERVED UNDER ACONITINE AND ON ELECTRICAL STIMULATION.

By ARTHUR R. CUSHNY.

(*From the Pharmacological Laboratory, University College, London.*)

IN 1897, the irregularities of the heart under aconitine were examined in my laboratory by Matthews¹², who demonstrated that in addition to stimulating the inhibitory mechanism, aconitine has a direct action on the heart muscle whose increased irritability is indicated by extrasystoles in the ventricles, and sometimes by independent rhythm in these chambers. Almost simultaneously with Matthews, Cash and Dunstan¹ described these features, and noted in addition that the auricle sometimes beat in only half the rhythm of the ventricle. Several other irregularities were observed.

The renewed interest in the irregularities of the heart suggested that the examination of those observed under aconitine might throw some light on some of the clinical forms, and with this object I have performed a number of experiments on animals with direct methods of recording the cardiac movements. In the course of the work it became necessary to observe the effects of electrical stimulation of the heart, and these observations have been incorporated in this paper.

The movements of the heart were recorded by means of a modified Roy-Adami myocardiograph² attached to the right auricle and ventricle, so that a simultaneous record of the contractions of these two chambers was obtained. The systole is recorded by a down stroke, the diastole by an upstroke in the tracings taken by this method. The upper tracing is from the ventricle in all the figures, the lower from the auricle. The time signal marks $\frac{1}{2}$ second. The experiments were made on dogs anaesthetised with morphine (subcutaneously) and paraldehyde (*per os*), and sometimes with a small amount of chloroform in addition. The carotid pulse was generally recorded by Hürthle's manometer, and aconitine was injected into the jugular or saphenous vein in .05 mg. doses. The vagi were cut in order to avoid the effects of the preliminary central stimulation. Tracings were taken by Brodie's kymograph, which was arranged to run at a slow rate during most of the experiment, but the speed of which was much accelerated at intervals so as to admit of the accurate analysis of any new phenomenon.

As a rule irregularity was induced by about 0.2 mg. of aconitine hydrochloride. In one case in which atropine had been injected previously 0.4 mg. was required, and in another in which the heart was weakened by long exposure, a larger amount than usual was also required. The forms

of irregularity were very varied in different animals and in successive phases in the same dog, agreeing only in the final fibrillation. Among these different forms, however, certain types were presented to which most of the others approximated more or less closely, and those types will be described here.

Reversal of beat. In nearly half of the experiments the first irregularity that occurred was a sudden change in the direction of the cardiac impulse,

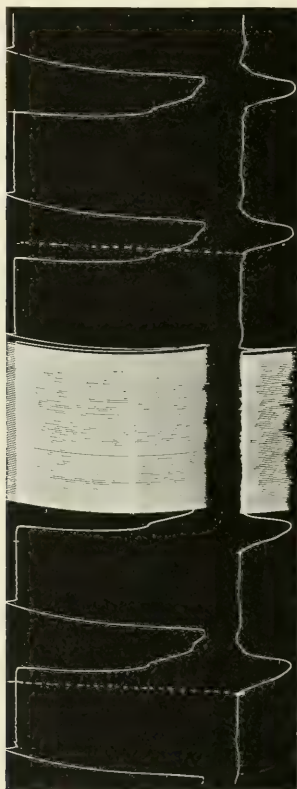


Fig. 1. $\times \frac{1}{2}$ linear. Reversal under aconitine. To the left, the auricular systole precedes the ventricular; in the middle is a period of slow drum during which reversal occurred, and to the right the ventricular systole begins before the auricular. The two dotted lines in the tracing are drawn to indicate the point in the ventricular cycle corresponding to the beginning of the auricular systole.

the ventricle beating before the auricle and imparting to the latter the impulse in response to which it contracted. This reversed beat induced surprisingly little change in the character of the tracing, the most noticeable alteration consisting in a slight weakness of the auricular contraction

accompanied by a more or less well-marked fall in blood pressure. The rate of the heart was little if at all accelerated, and the movements of both chambers were perfectly regular in rhythm. On watching the movements of the writing levers at this time, one got the impression that they descended simultaneously instead of the auricular preceding the ventricular. And on measuring the interval between the auricular systole and the next ventricular one (A-V interval) a great change was noted. Thus in the experiment from which Fig. 1 is taken the auricle normally preceded the ventricle by 0.07-0.08 sec., while after the reversal the ventricle preceded the auricle by 0.08-0.09 sec., so that the conduction in the reversed direction was slightly slower than in the normal. In none of my experiments did this reversal occur while the drum was running fast, and it is impossible to analyse the phenomenon accurately with slow running drums. In two instances, however, the change occurred during a comparatively short interval of slow drum (Fig. 1), and the beats could be counted. In these the ventricle was found to have contracted once less than the auricle. It is obvious, therefore, that in these cases an impulse descending from the auricle aroused the ventricle to contraction, and from this a wave returned to the auricle and caused an auricular beat. The auricle then remained quiescent until a second impulse from the ventricle, which had assumed its own independent rhythm, again aroused it.

The fact that the ventricular systole occurs before the auricular is not, of course, irrefragable proof that the rhythm is reversed, for it may be urged that the change is due to extreme slowness in the conduction through the

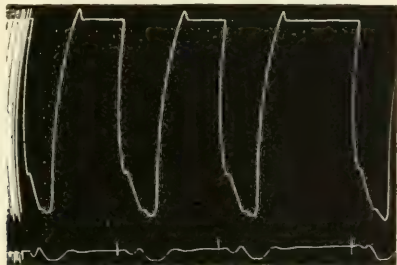


Fig. 2. $\times \frac{1}{2}$ linear. Reversal under aconitine from same heart as Fig. 1. The auricle continues to follow the beat of the ventricle and reflects the irregularity of its rhythm. The cross lines on the auricular tracing correspond in time to the beginning of ventricular systole.

auriculo-ventricular bundle, the impulse from one auricular systole only reaching the ventricle immediately before the next contraction of the auricle begins. In the instance given above this would necessitate the A-V interval changing from 0.07-0.08 sec. to 0.66 sec., but this does not seem impossible.

In some experiments this doubt could not be altogether resolved, but in that from which Fig. 1 is taken, and in several others, irregularities in the ventricular rhythm which occurred later were faithfully copied by the auricle, so that no further question is permissible. Thus, after the rhythm given in the later part of Fig. 1 had persisted for some 20 minutes, some quicker contractions occurred in the ventricle, and were immediately followed by the auricle (Fig. 2), and the V-A interval remained approximately equal though it was slightly shorter after the longer pauses, apparently from the conductivity of the A-V fibres having longer time to recuperate. Later in this tracing, the quick contractions of the ventricle became more numerous, as many as 5 or 7 intervening between the slower beats, but the auricle continued to follow the rhythm exactly. Still later, the ventricle assumed this quicker rhythm entirely, the auricle following suit. A gradual

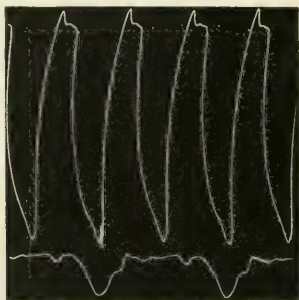


Fig. 3. $\times \frac{1}{2}$ linear. Reversal under aconitine; from same heart as Figs. 1 and 2. The auricle now beats only half as fast as the ventricle. The smaller oscillations on the auricular tracing are due to the mechanical shock of the ventricular movement. In Figs. 1, 2 and 3 the kymograph was moving at the same speed.

acceleration of the rhythm then set in, while the V-A pause became somewhat longer. Finally, the auricle responded only to every second beat of the ventricle (Fig. 3), but did so perfectly regularly. The conduction of the fibres of the auriculo-ventricular bundle was thus practically as good in the reverse direction as in the normal in the beginning, but later in the experiment became insufficient, either through the action of the drug, or, as seems more likely, because insufficient time for recuperation was allowed them as the impulses reached them more rapidly. Cash and Dunstan mention that the auricle often beats in 1 : 2 rhythm, but do not explain that the rhythm is reversed.

In other experiments in which reversal of the rhythm occurred, the

auricle continued beating with the ventricle in accelerating rhythm until delirium occurred. In a series of experiments formerly carried out in which the ventricle was stimulated by rhythmical electric shocks, the direction of the impulse was also reversed, as a general rule with only slight irregularity in the beginning, as also appears from the tracings of Fischel⁶. In one experiment, in which reversal was induced by electric stimulation of the ventricle*, every fifth impulse failed to reach the auricle³, just as in Fig. 3 every second impulse fails to pass the fibres, so that the resemblance between the reversal under aconitine and that under ventricular stimulation appears almost complete. In one feature only do they differ; when reversal is elicited by electrical stimulation the rhythm of the heart is, in my experience, always accelerated, and the reversal is explained by the impulses passing from the ventricle to the auricle, and thence to the rhythmic area round the veins, which cannot emit its normal impulses because its irritability is constantly abolished by these recurrent impulses. But in Fig. 1 there is no acceleration whatever in the reversed rhythm; one must, therefore, suppose that the first retrograde impulse reached the normal rhythmogenic area just before it would have discharged, and that each succeeding impulse reached it at a corresponding point, thus preventing the area from discharging, although no change in rhythm occurred; or it is possible that the area was suddenly depressed, though it seems unlikely that this accident should correspond so exactly with the point at which the ventricle became automatic.

In other experiments complete reversal of the rhythm was not attained until after a more or less prolonged period of irregularity in both ventricle and auricle. But when the ventricle became regular with a much accelerated rhythm, the auricle soon followed its rhythm satisfactorily. In this case the rhythm was shown to originate in the ventricle by the fact that the auricle relinquished its own slower and irregular rhythm and adopted the ventricular, which had in the previous irregular period shown no recognisable relation to that of the auricle. The latter now became perfectly regular, following each contraction of the ventricle after a definite interval.

It is important to note that when reversed rhythm has been developed, the record of the carotid pulse may show no change of any significance, as was the case in the experiment from which Fig. 1 is taken.

In reversed rhythm, the irritability of the ventricle is so augmented that it assumes a regular rhythm of its own, and this is transmitted to the auricle. In several experiments the irritability was increased, as was shown by independent idioventricular† contractions, but these were isolated and did not give rise to an independent rhythm, and they were not propagated

* It may be added that an isolated idioventricular contraction is not generally propagated to the auricle, merely because the impulse from the ventricle finds the auricle in the refractory phase.

† i.e., extrasystoles arising in the ventricle itself, and not propagated from the auricle.

to the auricle. These extrasystoles sometimes followed each normal ventricular beat, or two of them might be interpolated between two normal ones, and in fact every transition between isolated extrasystoles and independent ventricular rhythm might be seen in succession.

In one unpoisoned heart, after repeated stimulation of the ventricle with electric shocks and the application of iced saline, another form of irregularity was met with, which resembles reversal at first sight but differs from it in the fact that the ventricular and auricular systoles commence simultaneously (Fig. 4). On regular electrical stimulation of the ventricle this rhythm could be changed to regular reversed rhythm, in which the ventricular systole preceded that of the auricle by about 0.1 sec., thus showing that the original rhythm did not arise from the ventricle. And during the simultaneous rhythm the ventricle obviously did not derive its rhythm from

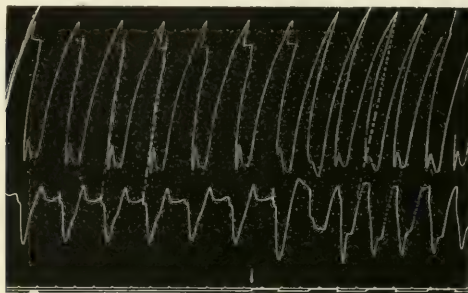


Fig. 4. $\times \frac{1}{3}$ linear. Simultaneous contraction of auricle and ventricle. At the point indicated by the signal electrical stimulation of the ventricle began and true reversed rhythm set in. The dotted lines indicate the point in the auricular cycle that corresponds in time with the beginning of the ventricular systole.

the auricle as in the normal heart, for there was no A-V pause, while before this form of contraction began and later towards the end of the experiment when the normal rhythm was reinstated there was a pause of 0.1 sec. between the auricular and ventricular systole. It seems to follow that the impulses arose at some point from which they were propagated to each chamber at the same rate, causing simultaneous contractions. Simultaneous contractions of the auricle and ventricle closely resembling these may in fact be obtained by passing a shock through the auricle and ventricle by electrodes, one of which is placed on the ventricle, the other on the auricle.

On passing a single electric shock through the ventricle during this

rhythm, a premature contraction of the ventricle was induced (Fig. 5). In the particular case observed the extrasystole was stronger than the preceding and subsequent contractions. It was followed by a long pause in diastole, after which the former rhythm was reinstated by a contraction which was weaker than those preceding the extrasystole*. The auricle, which had been contracting simultaneously with the ventricle, remained 0.16 sec. in diastole after the premature ventricular systole began and then contracted also, this contraction occurring prematurely. It then remained in diastole until the subsequent contraction of the ventricle, when it contracted simultaneously, thus restoring the former rhythm. The duration of the "bigeminus"† in each chamber was equal to two periods, the pause after the extrasystole compensating for its prematurity (see Fig. 5). The pause after the premature auricular systole was 0.16 sec. shorter than that

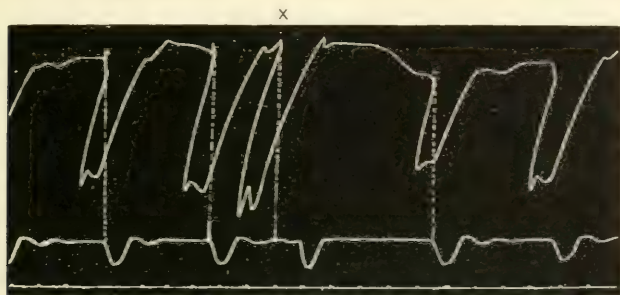


Fig. 5. $\times \frac{1}{4}$ linear. From same heart as Fig. 4. Simultaneous beat of auricle and ventricle. At X a premature systole, induced in ventricle by electric stimulus.

N.B.—The kymograph was running irregularly here, and equal times are not always indicated by equal lengths of the tracing.

following the ventricular, since the auricular contraction followed the ventricular after this interval. When the normal ventricle is excited to contract in extrasystole, the bigeminus is generally confined to the ventricle, and its duration is equal to two normal periods, because after the extrasystole the ventricle remains at rest until the impulse descending from the auricle at the normal time arouses it to contraction. When, however, the

* The weak contraction after the pause may perhaps be due to the distension of the ventricle, this more than compensating for the greater time for recuperation. The strength of the extrasystoles may be accounted for in the same way, the ventricle here contracting without encountering so much resistance from its contents.

† "Bigeminus" is used, as suggested by Hering, to indicate the period intervening between the contraction before an extrasystole and that following it.

extrasystole of the ventricle gives rise to an impulse which arouses a "retrograde" systole in the auricle, the bigeminus is generally shorter than two full periods*, apparently because the impulse travels to the rhythm-giving area at the base of the heart and disorganises it. In this abnormal rhythm, the impulse is retrograde, yet the bigeminus is not shortened, from which, according to the current views, it is to be inferred that the impulse fails to reach the point from which the rhythm arises. On the other hand an extrasystole arising in the auricle during this rhythm was not followed by a full compensatory pause, and, therefore, appeared to be propagated to the point giving rise to the rhythm. From the fact that an impulse passing from the ventricle to the auricle does not affect the point of rhythmic discharge in this rhythm, it may be inferred that the latter does not lie on the path of these impulses, i.e., is not situated in the auriculo-ventricular fibres or node, and equally the auricle and ventricle seem to be excluded from being the seat of the rhythm. I am at a loss to suggest how this form arises, unless from some point in the bundle, through which the retrograde impulse does not pass.

Irregularities from impairment of conduction in the auriculo-ventricular bundle. Some diminution in the rate of conductivity of impulses between the auricle and ventricle is very commonly met with under aconitine. It may be evidenced by some prolongation of the A-V interval, e.g., from 0.1 to 0.3 sec. under aconitine. Sometimes this prolongation of the interval gives rise to the appearance of the reversed rhythm, for the impulse may be delayed so long in the bundle that the ventricular systole begins only immediately before the next auricular one. Owing to this depression of the conduction an impulse may fail to pass, and the next A-V period is very short owing to the longer period allowed for recuperation of the fibres. A common irregularity under aconitine is half rhythm, in which the auricle beats fairly rapidly, but every second impulse fails to reach the ventricle, which, therefore, beats at only half the rate of the auricle. Or half rhythm may occur in inverted rhythm (Fig. 3), the ventricle beating rapidly and regularly, but only one of two impulses reaching the auricle, which accordingly contracts only half as many times per minute as the ventricle.

A recurring type of irregularity may be presented by hearts in which the conductivity is considerably impaired. For example, the period A-V may increase with each beat until the conduction fails altogether and no ventricular contraction follows the auricular; the next A-V period is very short, owing to the long pause for recuperation, the succeeding is somewhat longer, and the successive periods lengthen until a complete failure occurs again. This form of irregularity has been so frequently described in the

* If the auricular contraction occurs immediately before its normal position, the "bigeminus" may be very little, or not at all shortened, but in the case in point the retrograde auricular systole from a ventricular extrasystole occurred one-fourth of a period prematurely, yet the subsequent compensation was complete.

human heart in disease, and in animals from pressure on, or section of the auriculo-ventricular bundle that it is unnecessary to detail it further, but it is of interest to find it developed in poisoning in animals.

In two experiments there was complete block of the bundle, the auricle and ventricle beating in independent rhythms, and the periodic variations occurring which are so frequently seen under digitalis, and which occur in exceptional animals when the ventricle is stimulated by repeated electric shocks¹. In these cases under aconitine the independent ventricular rhythm was much quicker than it is in the unpoisoned heart in block. In fact it approached very nearly to the auricular rhythm.

Alternation in strength. One of the most common forms of irregularity under aconitine was alternation in the strength of the contractions. This sometimes gave rise to pulsus alternans in the carotid, but in other cases the difference between successive beats in the ventricle, while evident enough in the direct tracing, was too small to be observed in the pulse tracing; in others the weaker beat was insufficient to cause any wave whatever in the carotid, and the pulse tracing then presented a series of regular equal waves at one-half the rate of the ventricle.

The auricle beat quite regularly, and the ventricle followed it at a constant

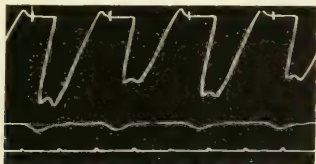


Fig. 6. $\times \frac{1}{2}$ linear. Ventricle under aconitine. Alternation in strength with constant rhythm. The auricle beat very weakly and regularly. The commencement of its systole is indicated on the ventricular tracing by cross lines.

interval. But the ventricular contractions alternated in character, one being strong, reaching full systole and relaxing slowly, while the next was weaker, and failed to reach full systole. On examining these more closely, e.g., by projecting one on the other, they are found to differ in other features than in their strength only (Fig. 6). The actual movement of contraction is found to occupy about the same time in each, apparent differences in this respect being probably due to throw of the lever. But the pause in full contraction is shorter in the weaker beat, relaxation being earlier, and although the diastole begins more gradually it is often complete earlier than in the stronger contraction. The heart then rests dilated until the next impulse reaches it, and full relaxation being attained between each beat, the variation is only in the degree of systole.

Alternation is generally more marked in the ventricle than in the auricle, but sometimes the ventricle is comparatively slightly affected, while the auricle shows marked alternation. Fig. 7 was derived from an experiment in which the rhythm was reversed, and in which gradual acceleration of the rhythm was occurring. The alternation affected not only the degree of systole, but, especially in the latter part of the tracing, diastole also, the stronger contractions being followed by much less complete relaxation than the weaker ones. In other words, the stronger beats were so prolonged that there was no time for complete relaxation before a new impulse induced renewed contraction, which was weak and short and allowed more time for relaxation. Somewhat later in this experiment the interval preceding the weak beat appeared to be longer than that following it, but it was impossible to be certain of this owing to the throw of the lever. The auricular tracing also shows alternation, the stronger contraction in it following the stronger in the ventricle, and the period V-A appearing to be constant. The auricular

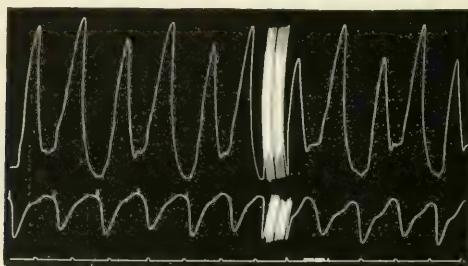


Fig. 7. $\times \frac{1}{2}$ linear. Alternation in ventricle and auricle under aconitine.

contraction is much weaker than before aconitine was injected, but is stronger than usual during alternation from this drug. The impulse to contraction here arose in the ventricle itself, and the fact that it appears to be regular indicates that the spontaneity or irritability of the ventricle did not vary in the same sense as its contractility. Later in this tracing the alternation gradually lessened and disappeared, the rate of the beat remaining constant at 257 per minute. The rhythm then rose to 286, and the alternation returned.

This alternating type is generally preceded by some change in the rhythm which demands greater exertions from the ventricle, as for example, if the rhythm changes from $\frac{A}{V} = \frac{1}{1}$, in which no alternation is present, to regular $\frac{1}{2}$ rhythm, with perhaps a rather slower A rhythm, or if the rhythm of both auricle and ventricle is suddenly doubled. In other cases it

follows from some previous irregularity, such as a series of extrasystoles. Sometimes the change is a progressive one, the difference between successive beats at first being barely perceptible, but increasing gradually until it becomes very striking. The alternation often lasts for many minutes without further change; thus I have recorded it for half an hour, the tracing at the end of that time being identical, except in minor details, with that at the beginning, and no further irregularities having occurred in the interval.

Alternation in the strength of the contractions may sometimes be elicited in the unpoisoned heart. That from which Fig. 8 is taken had been exposed for about two hours, and had been subjected to repeated electrical stimulations and to prolonged cold. The auricle finally ceased contracting, and the ventricle beat spontaneously at the rate of about 20 per minute. The beats were equal in strength. Electric make and break shocks were now passed through the ventricle at the rate of 160 per minute, and the rate rose to 80 per minute, i.e., the ventricle responded with a contraction to every second break shock, the make having no effect. The

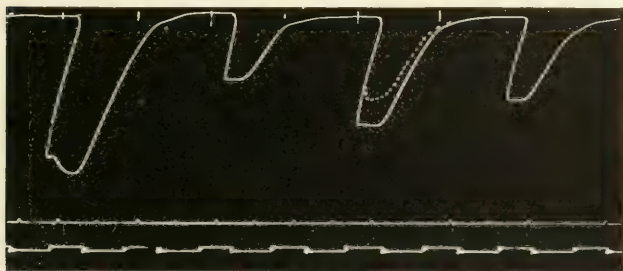


Fig. 8. $\times \frac{2}{3}$ linear. Alternation in the ventricle from rapid electrical stimulation.

contractions were alternating in strength, strong prolonged contractions intervening between weaker and shorter ones. I have drawn in dotted outline the curve of one of these weaker contractions superposed on one of the stronger, showing that, while the downward stroke of each coincides in time, the period from the end of this phase is somewhat longer after the weak contraction than after the strong. This tracing is also of interest in the fact that it shows the extreme "hypodynamic" condition of the heart. For the same strength of shock was sufficient earlier in the experiment to induce renewed contraction in the ventricle, when it reached it at the beginning of the relaxation; but here it fails to induce contraction even when full relaxation has been reached. It may be concluded that at this time the

heart had not recuperated so much at the end of its relaxation as previously at the beginning of diastole.

Pulsus alternans or alternation in the strength of the pulse has been known clinically since Traube¹⁵ described it in 1872, and has received increased attention in the last few years¹⁴. It has always been attributed to variations in the strength of the ventricular contractions, and Hering⁹ has confirmed this by tracings taken from the apex beat. In a recent publication⁹ Hering states that the stronger beats in the cardiogram may correspond with the stronger of the pulse or with the weaker, and that if two cardiograms be taken simultaneously the one may correspond with the pulse, while the other exhibits large excursions with the weak pulse and smaller ones with the stronger pulse.

The statement is frequently made that it occurs in animal experiments under a number of conditions, varying from simple perfusion of the heart with Ringer's solution to poisoning with members of the digitalis series and with glyoxylates. In many cases, however, the observers do not seem to have differentiated between the true alternation (Hering), in which the rhythm is regular, and a continuous bigeminus, in which the weaker beat is preceded by a shorter pause than the stronger one. And in most published tracings it is impossible to measure the intervals exactly owing to the slowness of the kymograph used. It has been stated recently by Starkenstein and Hering that under the glyoxylates, pulsus alternans is elicited fairly regularly; but with this possible exception, it may be doubted whether any poison has yet been shown to have a specific action in this direction, as distinguished from its altering the rhythm of the heart.

The current view as to the causation of clinical pulsus alternans was given by Wenckebach, who based his explanation on the results obtained by Hoffmann in the frog. The latter showed that in a feeble heart a weak beat is not only low in strength but also short in duration, and, therefore, permits of a longer period for recuperation than a stronger beat, which lasts longer, and thus, by encroaching on the recuperative period before the next beat, tends to weaken it. This weak beat is correspondingly short in duration, and, allowing a long recuperative period, is again followed by a stronger systole, and in this way alternation may continue, each strong beat leading to a shortened recuperative period, and thus to a weak and short beat, which in turn permits of a more complete recovery, and consequently to a stronger contraction.

Muskens¹³ suggests that the alternation in the frog's heart under digitalis arises from some of the fibres responding only to every second impulse, the movement of the lever thus arising alternately from the whole musculature and from a part. This he supposes to result from a failure of the conduction in the ventricle recurring with each alternate impulse. A similar view has recently been put forward by Hering to explain the alternations after glyoxylates in mammals; he considers that at the time of the weaker contraction a partial systole occurs. This view does not seem to be

inconsistent with that of Wenckebach and Hoffmann, which is also supported by my results.

The development of alternation may sometimes be observed easily in the dog's heart in the course of a long experiment. When an extrasystole is elicited in the recently exposed ventricle, the irregularity ceases after the "post-compensatory" contraction, which is very powerful and very prolonged. At the end of a long experiment on the other hand, the powerful, prolonged post-compensatory contraction is followed by a weak and short beat, this again by a longer and stronger one, and this alternation may persist for 5-10 beats or more. During the course of the experiment, therefore, the heart must have undergone some change, which materially alters the re-action to the same stimulus, and it is necessary to differentiate between the immediate stimulus which leads to a manifestation of the alternation and the underlying condition, of which this anomalous contraction is a symptom. Similarly, the ventricle from which Fig. 9 was derived had not manifested alternation in strength until the series of stimuli accelerated its rhythm, when it immediately gave this characteristic tracing. This ventricle had previously been contracting much more rapidly, and, when in the beginning of the experiment (see Fig. 4) a series of shocks were given, it accelerated from 130 to 190 per minute without any alternation. Yet in its exhaustion at the end of the experiment a rate of only 80 per minute was sufficient to elicit this symptom.

In patients it is frequently noted that *pulsus alternans* is elicited by exertion, and in my experiments a gradual acceleration was often accompanied by an increased disparity in the contractions, while the alternations in one case disappeared when the rhythm was slightly slowed. On the other hand, in the heart from which Fig. 8 was taken the alternation gradually disappeared, the rhythm remaining unchanged; but it returned again upon the occurrence of further acceleration.

In every case in which alternation occurs under poisons, it is therefore necessary to inquire, how far this effect may be due to the poison increasing the rhythm or the irritability of an organ exhausted by exposure, cold or other conditions, and how far the poison itself induces the exhaustion. Several of the drugs, which have been said to induce alternation, such as the digitalis series and aconitine, undoubtedly increase the irritability in the later stages of poisoning; and from my experience, in which digitalis rarely induces true *alternans* in mammals, I am inclined to regard this as the explanation in the case of this drug. After aconitine, alternation occurs much more frequently, and here, and probably also in the case of the glyoxylates, the poison may induce exhaustion, besides causing greater demands to be made on the heart by the augmented irritability. When the character of this exhaustion is inquired into, a difficulty is met at once in the fact that alternation is not regularly induced by any known means, unless by glyoxylates. It is not identical with weakened contractile power, for when chloroform is given early in an experiment, until the auricle ceases

and the ventricle is in the last stages of weakness, an electrical shock gives rise to an extrasystole without any subsequent alternation*.

In the tracing given in Fig. 8 the ventricle responded only to every second break shock; yet the shocks, to which it failed to respond, reached it after it had attained full diastole, i.e., at a point at which the normal unexhausted heart responds with a contraction little, if at all, weaker than the normal one. In other words the recuperation of the heart is very much slowed, and in this seems to lie the essential difference between the heart in which alternation does not occur and that in which it is readily elicited by anything demanding an accelerated rhythm. As the normal ventricle begins to relax it also begins to recuperate its energy, and before the next impulse arrives it has practically recovered from the previous contraction. This is shown by the fact that a slightly premature stimulus arouses a contraction which is almost equal in strength to one occurring at the normal interval, i.e., the recuperation is so rapid that the ventricle has a certain amount of reserve on which it can draw without serious detriment to the strength of the contraction. If the recuperation is retarded however, a stimulus reaching the ventricle only slightly earlier than usual causes a much greater departure from the normal, both in the strength and the duration of the contraction. It arouses the ventricle when it is still in a very imperfect stage of recovery and when every additional moment adds materially to its stock of energy. Thus, in Fig. 8 the first contraction was preceded by a prolonged pause, and it is noteworthy that even the stronger of the subsequent contractions fell very much short of it in strength, i.e., the process of recuperation was still actively progressing when the impulses aroused contraction. And the difference between the first contraction and the subsequent ones was greater than occurs in unexhausted hearts after a similar pause, because in these the recovery is more rapid and the prolongation of the normal pause adds less to it. If the rhythm of the heart becomes slower, the prolongation of the time of recuperation compensates for its slowness, and the alternans disappears. If, as is apparently the case with chloroform, the rate of recovery is not so much affected as the strength of contraction, the latter may be reduced to a very considerable extent without the "exhaustion" condition arising, and no alternans will result.

Starkenstein believes that alternation arises from a disturbance of contractility which results from previous stimulation, and cites as examples the effects of the digitalis series. But these are not, in my experience, especially prone to induce true alternation, and in any case they cause acceleration of the heart in the later stages, and thus offer favourable conditions for the manifestation of alternans. Straub has shown that under antiarin the refractory phase is prolonged in the frog's heart, but the tracing given in his paper is not that of a true alternans as Starkenstein supposes. And

* Starkenstein has pointed out that chloral also fails to induce alternans in the frog.

the action of members of the digitalis series in prolonging the systole in the frog is so different from their effects in the mammal that deductions from the one to the other can only be made with the greatest reserve.

A combination of this delayed recuperation with imperfect conduction through the auriculo-ventricular bundle is shown in a number of tracings, which at first appear to be extremely complicated. The form presented in Fig. 10 repeated itself with small variations for some time, and occurred in the same heart as Fig. 6. The auricle beat regularly, and each

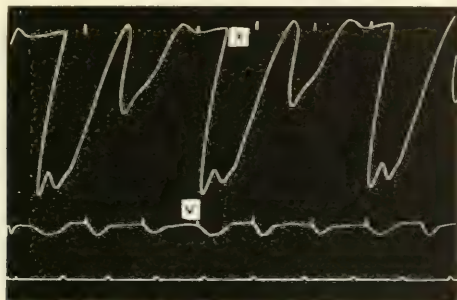


Fig. 9. $\times \frac{2}{3}$ linear. Alternation combined with imperfect conduction. The marks along the ventricular curve indicate the time of the beginning of systole in the auricle.

ventricular contraction was the response to a previous auricular one. Thus, the ventricular systole at X was in response to the auricular V, and the ventricle having been at rest for some time, the A-V interval was short, and the ventricular contraction was strong and prolonged. The next ventricular

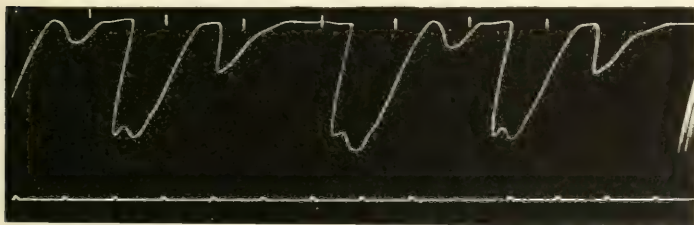


Fig. 10. $\times \frac{2}{3}$ linear. Alternation combined with imperfect conduction.

systole followed later from the exhaustion of the conduction, and was weak from the exhaustion of the contractility: the third auricular impulse failed to

pass, and there was a corresponding recovery of the conduction, and also of the contractility before the fourth impulse arrived and the anomaly recommenced.

Similar anomalies are presented in Figs. 10 and 11, taken from the same experiment, in which the beginning of the auricular systole is indicated by the perpendicular lines in the tracing from the ventricle. Some time later the ventricle suddenly changed to half rhythm; and, more time for recuperation being allowed, the beats became regular in strength and in the duration of the A-V interval.

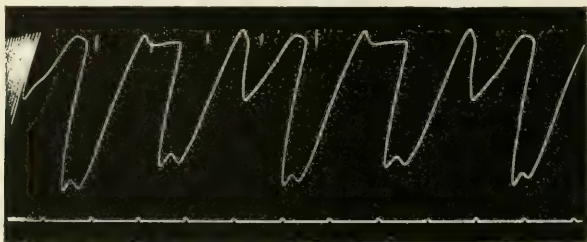


Fig. 11. $\times \frac{2}{3}$ linear. Alternation combined with imperfect conduction.

Continuous bigeminus. Another form of irregularity which is liable to be confused with the alternation, and which frequently occurs under poisonous doses of aconitine and digitalis, has been termed by Hering continuous bigeminus. It appears most frequently under aconitine when the rhythm is slow, and is characterised by each normal beat of the auricle being followed by an extrasystole which induces a similarly premature ventricular contraction (Fig. 13). The extrasystole is much weaker than the normal beat in both auricle and ventricle, owing to the early point in the recuperation period in which it occurs. It is followed by a long pause, and then by a normal auricular and ventricular contraction. The interval between the auricular and ventricular contraction (A-V) is longer in the case of the extrasystole than in the normal, indicating that the conductivity of the auriculo-ventricular bundle is imperfectly repaired in the short interval.

This extrasystole thus presents all the characteristics of those of auricular origin, and arises from some normally inactive point, which has acquired the property of discharging impulses, and which preserves the same rhythm as the original rhythmic area; for the extrasystole follows at a definite time after each normal contraction, just at the time when the functions of the heart are at their lowest ebb owing to the previous contraction. A plausible view to account for this is that the second rhythmic point is aroused to

discharge an impulse, by the original contraction, i.e., that the normal impulse sweeping over the heart from the normal rhythmic area reaches some point at which it awakes a fresh discharge, and this second discharge gives rise to the extrasystole.

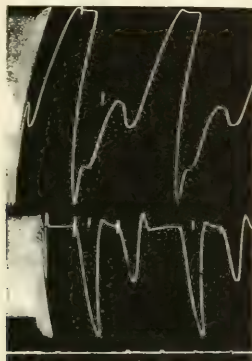


Fig. 12. $\times \frac{1}{2}$ linear. Continuous bigeminy under aconitine.

This view is supported by a sudden change which occurred in one of the experiments in which this form was observed (Fig. 13). The rhythm suddenly changed to one exactly three times as fast as that described, but the same pairing of the beats remained, only now there were three pairs in

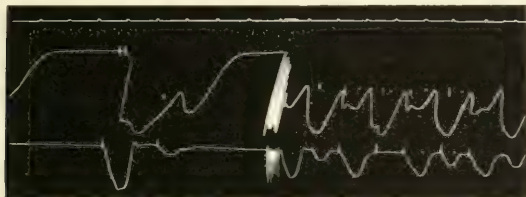


Fig. 13. $\times \frac{2}{3}$ linear. Continuous bigeminy with sudden acceleration to a rhythm three times as fast.

the time formerly occupied by one. Here, I take it, three impulses reached the auricle from the original rhythmic area instead of one, and each of these was followed by its satellite extrasystole as before.

In this tracing one is at once struck by the extreme feebleness of the auricular extrasystole during the slow rhythm. It is obvious that the exaggerated irritability is accompanied by great impairment of contraction, i.e., that the exhaustion which in other tracings is betrayed by alternation is here present. On acceleration to three times the rhythm the extrasystole of the auricle is not weaker but rather stronger, and it follows sooner after the normal beat. This improvement in the strength of the extra beat may probably partake of the nature of the staircase phenomenon of Bowditch, and the same may be true of its more rapid occurrence after the normal contraction. In the later part of the tracing it is noteworthy that the weak beat is preceded by a longer interval (counting from the beginning of systole) than the stronger, so that according to the canon of Hering it would not be considered an extrasystole, but an alternans. Its development from the preceding form, however, indicates its character, though the exhaustion and delayed recuperation which is sometimes manifested in alternation is also present. It is noteworthy that this exhaustion of contractibility is here associated with an extraordinary degree of irritability, leading to extrasystoles during a rhythm of 138, and thus to 276 contractions per minute.

In another form of the same type the auricle beats regularly, but each beat of the ventricle is followed by a weak premature contraction, which arises from some point beneath the contractile area of the auricle—either from the ventricle itself or from the auriculo-ventricular bundle. The new rhythm-giving area, therefore, may lie in the auricle, or in the ventricle, or possibly in the intermediate structure.

In tracings taken from the radial artery in man each normal wave is sometimes followed by a secondary one (continuous pulsus bigeminus) (Hering). The extrasystole which gives rise to this secondary wave is sometimes so persistent and follows with such regularity, that the suggestion of a secondary rhythmic focus aroused to activity by the original wave is suggested. In other cases, the extrasystole occurs regularly after every third normal pulse, and here the secondary focus may have a rather longer period of recuperation. In this case it is to be presumed that this focus has not its irritability exhausted by each beat, perhaps because the descending impulse fails to reach it, but goes on accumulating energy until it finally reaches the exploding point, this occurring after each third or more beats arising from normal focus.

Abnormal sino-auricular conduction. I have already stated that under aconitine the conduction in the auriculo-ventricular bundle is often impaired, as is shown by prolongation of the A-V interval and half rhythm, which may persist for some time and then give way to the normal rhythm with the ventricle beating at twice the rate.

When the auriculo-ventricular bundle is affected, these changes affect only the ventricle, but in a number of instances a somewhat similar change is seen in the auricle, whose rate may suddenly be doubled or halved, the

ventricle following its rhythm exactly. This is different from the phenomenon described already as "continuous bigeminus" for the contractions of the auricle may be equal in strength and at equal intervals in time*. It may, however, be superposed on a continuous bigeminus, as is seen in Fig. 13. It sometimes leads to alternation in strength in the auricle and still more often in the ventricle, whose contractility may not be equal to the demands made on it by the more rapid rhythm. Or, when alternation has already occurred, the rhythm may be reduced to one-half, and the alternation disappears or becomes less marked as the contractility is now on a more equal footing with the rhythm. When the sudden acceleration occurs, the contractions of the auricle frequently become weaker, owing to the shorter time allowed for recuperation.

This phenomenon may be due to the rhythm-giving area emitting double or half the number of impulses to the auricle, or on the other hand, the actual number of impulses emitted may remain unchanged, but the number actually reaching the contractile elements may be altered. It being impossible to register the actual emission of impulses, but only the effect of those which reach the auricle, the question cannot be directly solved. On the analogy of the relation between the auricle and ventricle, one would be inclined to postulate the existence of some tissue connecting the rhythm-giving area to the auricle, corresponding to the auriculo-ventricular bundle and undergoing corresponding variations in conductivity. It seems unlikely that the area itself suddenly doubles its rhythm, for this would be without any analogy. If its irritability were increased one would expect rather a gradual quickening in its rhythm with a corresponding acceleration of the contractions. On the other hand the regularity of the beats precludes the view that one-half of them arise from the development of some subordinate rhythmic discharge such as I have discussed under continuous bigeminus. Engelmann observed in the frog's heart occasional failure of the auricular contraction, which pointed to a failure of the conduction from the vena cava to the auricle, and Wenckebach has utilised this observation to explain certain forms of irregularity of the heart in disease in man, and in a later paper¹⁶ supports this view by jugular tracings, which show absence of auricular contractions at intervals, while the general rhythm is preserved. Hering¹⁷ found the same occasional failure of the auricular contractions in a rabbit and dog, the auricular pause corresponding in length to two normal periods, and, therefore, to be ascribed to failure of an impulse to cause contraction. The sudden changes in the rhythms seen under aconitine seem to be further examples of this anomaly, and it is of interest to find that aconitine also impairs the conduction of the fibres of the auriculo-ventricular bundle.

In these cases the change in auricular rate was a sudden one, and took place without any irregularity making its appearance. In one experiment the auricular (and ventricular) rhythm was finally doubled, but the transition

* An instance of sudden change in the auricular rhythm is offered in Fig. 6, which was taken 53 secs. after Fig. 9.

phase was the more gradual one presented in Figs. 12, 14 and 15. Here a series of normal contractions was suddenly interrupted by the appearance of extrasystoles following each contraction of the auricle, and being propagated to the ventricle (Fig. 12). This appeared to be a continuous bigeminus in which each normal auricular contraction was followed by an extrasystole arising from an impulse generated in the auricle. The period between the weak beat in Fig. 12 and the following stronger one is equal to the period

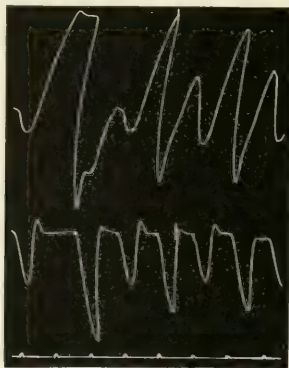


Fig. 14. $\times \frac{1}{2}$ linear. Acceleration of the rhythm to double rate with irregularity. Taken one second after Fig. 12.

prevailing previously in the normal rhythm. In the middle of Fig. 14, which began one second after the end of Fig. 12, the long pause after the auricular extrasystole was replaced by a comparatively short one, because the impulse from the rhythmic area now occurs at half the former interval. Alternate

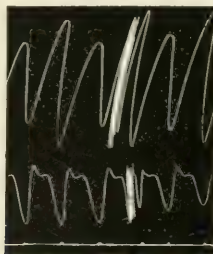


Fig. 15. $\times \frac{1}{2}$ linear. Rhythm now regular and double that prevailing before the irregularity was developed. Taken four seconds after Fig. 14.

extrasystoles of auricular origin still persist throughout Fig. 14, as is seen by the short interval before the weaker beat. Finally, in Fig. 15 the impulses

to contraction are all derived from the rhythmic area, and the auricle becomes regular. Alternation persists in the ventricle, and it is difficult to determine from its tracing alone when the premature contraction develops into the rhythmical.

Here again there is evidence of the arrival in the auricular contractile substance of twice as many impulses as previously, and the question arises whether these were developed previously but failed to reach the auricle, or whether the number of impulses developed was now doubled. In favour of the latter it may be urged that if the impulses were previously developed but were unable to reach the auricle, this must occur normally, for the previous rhythm was that before aconitine was given. On the other hand it is difficult to conceive of the number of impulses formed undergoing sudden duplication.

One of the most striking features in the irregular phase of the heart's action under aconitine is the large variety of forms assumed, so that the course is never the same in two hearts. Yet the etiology of these various forms may be reduced to two factors; aconitine retards the recuperation of the contractile and conductive power, while it increases the tendency to spontaneous movement, i.e., augments the irritability of each part of the heart. The latter factor is essential to the production of most of these forms of irregularity, for the delayed anabolism alone is incapable of causing most of these. Thus, long periods of regular contraction may follow some form of irregularity, if the rhythm is slower, i.e., though the contractility and conductivity are seriously impaired, yet they are capable of regeneration, at the slow rhythm prevailing, and thus the beats remain regular. Any acceleration, however, is sufficient to induce irregularity, the impaired functions being unable to respond to the greater demands on them. Digitalis and its allies, including calcium and barium, also give rise to irregularity in movement when large quantities are administered. Here the contractile function is distinctly increased, but there is reason to regard the conduction as less augmented, and the irritability is very much greater than usual*. The earliest irregularity induced is generally the result of failure of the conduction through the bundle fibres, the auricle and ventricle beating in different rhythms. And later, most or all of the features may be reduced to this factor together with the exaggerated irritability with which the contractility, even though augmented, cannot cope. In aconitine poisoning the function of irritability seems to be augmented, while those of contraction and conduction are decreased, and this might suggest that these functions are incorporated in different anatomical units, and thus prove an argument in favour of the neurogenic theory. But the strength of the argument is broken by considering that under digitalis the contraction power is increased along with the irritability, while the conduction is not increased and may be diminished.

* The interaction of these effects is largely concealed in the therapeutic use of digitalis by the inhibitory stimulation, and can be best elicited in animals in which the vagus has been divided and atropine injected.

And under caffeine, irritability, contraction, and conduction seem to rise together, for irregularities seldom arise from the failure of the two last. And similarly, under chloroform all three seem reduced in equal measure. One must, therefore, hold that each function may be affected independently of the others by different drugs. And the variety of the forms of arrhythmia in different hearts shows that each individual organ varies in the susceptibility of its different functions.

CONCLUSIONS.

Under aconitine, many forms of irregularity of the heart occur, but most of these may be reduced to certain types.

- (1) Reversed rhythm, in which the impulse to contraction is generated in the ventricle and spreads upwards to the auricle.
- (2) Impaired conduction through the auriculo-ventricular bundle, which may lead to partial or complete block in either direction.
- (3) Alternation in the strength of the contractions in auricle and ventricle.
- (4) Extrasystoles in auricle or ventricle which sometimes occur at regular intervals (continuous bigeminus).
- (5) Sudden changes in the rhythm of the whole heart.

Two or more of these types may be present simultaneously.

Aconitine has a greater tendency to cause *pulsus alternans* than most other poisons, and this is ascribed to its production of exhaustion, and of delayed recuperation of contractility. Other drugs may induce *alternans* in a damaged heart by increasing its irritability, and thus making demands which the contractility is unable to meet.

Other forms of irregularity were observed in unpoisoned hearts under the influence of cold and electrical stimulation and are described.

BIBLIOGRAPHY.

- ¹ CASH and DUNSTAN. Phil. Trans. Roy. Soc., 1898, CXCB, 239.
- ² CUSHNY and MATTHEWS. Journ. of Physiol., 1897, XXI, 213.
- ³ CUSHNY. Journ. of Physiol., 1899, XXV, 62.
- ⁴ CUSHNY. *Ibid.*, 49.
- ⁵ ERLANGER. Journ. of Exper. Med., 1905, VII, 1; Amer. Journ. of Physiol., 1906, XVI, 160.
- ⁶ FISCHEL. Archiv f. exper. Path. u. Pharmak., XXXVIII, 228.
- ⁷ HERING. Archiv f. d. ges. Physiol., 1905, CVIII, 267.
- ⁸ HERING. Prag. med. Wochenschr., Feb., 1904, XXIX.
- ⁹ HERING. Münch. med. Wochenschr., 1908, No. 27.
- ¹⁰ HERING. Zeitschr. f. exper. Path. u. Therap., 1906, III, 511.
- ¹¹ HOFFMANN. Archiv f. d. ges. Physiol., 1901, LXXXIV.
- ¹² MATTHEWS. Journ. of Exper. Med., 1897, II, 593.
- ¹³ MUSKENS. Journ. of Physiol., 1907, XXXVI, 104.
- ¹⁴ STARKENSTEIN. Zeitschr. f. exper. Path. u. Therap., 1907, IV, 1 (literature cited).
- ¹⁵ TRAUBE. Berl. klin. Wochenschr., 1872, 185.
- ¹⁶ WENCKEBACH. Archiv f. Anat. u. Physiol., 1906, Phys. Abth., 323.

NODAL BRADYCARDIA.

BY JAMES MACKENZIE.

I. THE MEANING OF THE TERM "NODAL RHYTHM."

THE normal succession of events in a cardiac revolution, where a stimulus arising in the great veins provokes a contraction of the auricle followed by a contraction of the ventricle, is so well recognised, that it has been long looked upon as the only way in which the heart can carry on its work. Experiments had shown that by stimulating any part of the heart, so as to render that part more excitable than the normal starting place, the contraction of the heart would start from that part. It had also been shown that if a series of electrical stimuli were thrown into the ventricle at a rate slightly faster than the normal rate of the heart, a succession of cardiac contractions starting at the ventricle could be obtained; but an abnormal rhythm of this nature, arising spontaneously in the heart, had not been considered possible. More exact observations and more careful study of human irregularities have demonstrated, however, that the heart's contraction may start continuously from several places, and experiment has corroborated these observations (this *Journal*, page 1). The recognition of these abnormal rhythms in the human subject becomes possible only after the nature of the movements in the jugular veins are understood. Two distinctive forms of the jugular pulse have long been recognised; one where the contraction of the auricle causes a distinct wave preceding the ventricular systole, the auricular form of venous pulse (see Figs. 1, 8, and 16); and one where the auricular wave is absent, but where there is one large wave synchronous with and due to the systole of the right ventricle, the ventricular form of venous pulse.

Until 1893 this ventricular form of venous pulse was looked upon merely as an evidence of tricuspid regurgitation. Since that time it has been gradually recognised that it has a further significance. The presence of the ventricular venous pulse implies that the auricle no longer contracts at its normal place in the cardiac cycle. Clinical support for this view is found in the fact that synchronous with the appearance of the ventricular form of the venous pulse all other evidences of the auricular systole at the normal position in the cardiac cycle disappear; for instance, the disappearance of a mitral or tricuspid presystolic murmur when there is mitral or tricuspid stenosis, the disappearance of a wave in the apex tracing due to the contraction of

the right or left auricles, the disappearance of a wave in the liver pulse due to the systole of the right auricle.

For reasons to be given later it will be shown that in all probability the auricles and ventricles contract simultaneously.

In order to distinguish this abnormal rhythm I have called it the nodal rhythm. In my earlier papers on the subject I had called it the "ventricular rhythm," inasmuch as usually the ventricular contraction precedes the contraction of the auricle by a brief interval. I found, however, that the term "ventricular rhythm" had already been employed to describe the independent contraction of the ventricle, which occurs in heart-block. Though the condition I am about to describe has some affinity to this ventricular rhythm of heart-block, yet it is so very distinct in other respects that a special term is needed. As I have reasoned that the stimulus for contraction arises in an area which can start off ventricle and auricle together, it was suggested that this part may be the node of tissue from which the auriculo-ventricular bundle runs; and to the abnormal rhythm supposed to arise from this tissue the name of "nodal rhythm" is provisionally given.

I have collected many hundreds of cases of nodal rhythm, and although they all show a common feature, namely, the disappearance of the auricular systole from the normal period of the cardiac cycle, in subjecting them to analysis I find that there are features peculiar to limited numbers, so that one can divide them into groups more or less distinctive. It is with one of these groups I propose to deal in this communication.

In the vast majority of cases, where the nodal rhythm is present, the heart's action is at first more rapid than normal, sometimes excessively so. But there is a class of case where, so far from the rate of the contraction being more rapid than the normal, it becomes slower, and sometimes very markedly so. In most other respects the character of the heart's action corresponds to the more common forms of nodal rhythm, but if, as seems probable, these commoner forms owe their inception to disease rendering some part of the heart, such as the node, more excitable, this cannot hold good when the rate is much slower than that of the normal rhythmic area. Hence a search has to be made for some other cause. Facts pointing to a definite cause may appear when all the features connected with these cases are studied, and are compared with the results of experiment. In the following pages I give, first a brief account of some illustrative cases dealing only with the features that bear upon this abnormal rhythm, and then discuss some of the characteristics of these cases, and refer to the physiological and pathological conditions that may underlie this rhythm of the heart.

II. FOUR CASES OF SLOW NODAL RHYTHM, TWO OF WHICH PRESENTED EPILEPTIC MANIFESTATIONS.

Case 1.—Old rheumatic affection of the heart, with long continued impairment of the A-V bundle, with a delay between the As and Vs. Sudden inception of a slow and irregular action of the heart, with disappearance of all evidences of auricular contraction, at first transient, later permanent.

The first case to which I refer has been under observation for a period of over twenty-five years, and I have dealt more fully with the symptoms elsewhere³.

Male, born in 1851. I attended him for an attack of rheumatic fever in 1883. He was left with a damaged mitral valve, and when I took tracings of his jugular pulse in 1892 there was a delay in the interval between As (auricular systole) and Vs (ventricular systole), as shown by the increased *a-c* interval. With the exception of a short period in 1897, when he had an attack of heart failure with slight heart-block, his heart was perfectly regular at all times, until April, 1904. Fig. 1 is typical of the tracings of his

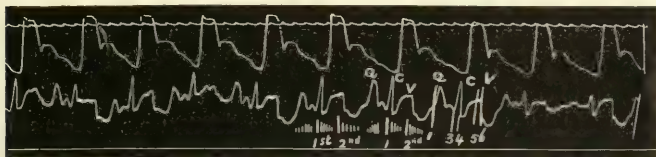


Fig. 1. Simultaneous tracings of the radial and jugular pulses. The rhythm is regular, and the auricular wave, *a*, precedes the carotid wave, *c*, though the *a-c* interval is greater than normal; *v* is the ventricular wave. The time marker records $\frac{1}{2}$ sec. in all tracings.

The perpendicular lines have the same significance in all the tracings. 1, indicates the beginning of auricular systole; 2, the beginning of the ventricular systole; 3, the beginning of the carotid pulse; 4, the beginning of the radial pulse; 5, the time of closure of the semilunar valves; 6, the time of opening of the tricuspid valves. The shading underneath represents the time of the murmurs present. Compare this tracing with Figs. 2 and 3. (W.H., 29th November, 1903.)

radial and jugular pulses up to that date. The rhythm is regular, the rate 60, and there is a well-marked wave, *a*, in the jugular tracing due to the systole of the auricle. Tracings from the apex beat always showed a well-marked wave, due to the systole of the left auricle. During the later years a well-marked murmur at the time of the auricular systole was always present, and also a murmur during the ventricular systole, and another at the early period of diastole (see shading in Fig. 1).

On the 19th April, 1904, he called as usual to report himself (he was following his trade as a mechanic, and performing heavy bodily labour), and I found his pulse continuously irregular and much slower with long

pauses. Tracings from the neck showed an absence of all evidences of the auricular wave, and the auricular wave was also absent from his apex tracings. The murmur which had hitherto been so marked a feature, preceding the ventricular systole, had disappeared, and there now remained the murmur during the ventricular systole, and the diastolic murmur, the latter followed during the long pauses by a silence lasting till the

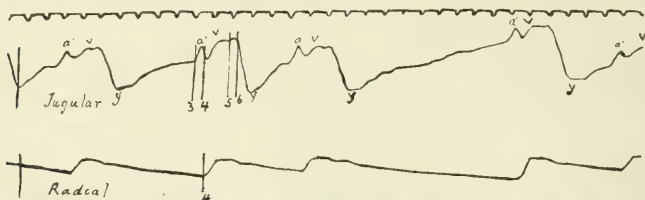


Fig. 2. Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular form, there being no auricular wave preceding the perpendicular line, 3. The wave *a'* occurs at the same time as the carotid pulse, and is probably due to the systole of the auricle contracting at the same time as the ventricle. The whole heart sometimes stands still for a long period; in the tracing there is shown a pause nearly twelve-fifths of a second in duration. (W.H., 1908.)

first sound (see shading under Fig. 3). The irregular and slow rate is shown in Fig. 2. This irregular action of the heart continued till the 26th April, when I found his heart quite regular and the auricular wave present as in Fig. 1. The auricular systolic murmur was also present. This action of the heart continued till November, 1904, when the heart's action again took on the irregular and slow rate, accompanied by the disappearance of all the evidences of the action of the auricles (as shown in Fig. 2). The patient was not conscious of any change in his heart's action,



Fig. 3. Simultaneous tracings of the jugular and carotid pulses, showing the synchronism of the wave *a'* with the carotid pulse. The shading underneath represents the time of the murmurs in the cardiac cycle. Compare with Fig. 1. (W.H., 1908.)

nor has this abnormal action incapacitated him in any way, for he has continued his work uninterruptedly (1909).

In the jugular tracings from this patient while the normal rhythm prevailed there was always a well-marked carotid wave (*c* in Fig. 1.). When the nodal rhythm occurred a small wave was present at exactly the same time as the carotid (perpendicular line 3 in Figs. 2 and 3). I have never been able to satisfy myself whether this was due to the carotid impact, or whether it was a wave in the vein, corresponding to the wave *a'* in the tracings from cases 2 and 3. I incline to the latter view, for in other cases I have observed this wave, *a'*, exactly synchronous with the carotid pulse, and its presence could be detected in the pulsation of the veins on inspection.

Case 2.—Sudden inception of nodal bradycardia, lasting for about three weeks.

Male, born 1852, a stout healthy-looking individual. I had known him for about twenty-eight years, and had attended him at various times for trivial complaints, and in 1903 for an attack of erysipelas of the face. He had enjoyed good health, was getting fat and somewhat short of breath. On the 9th November, he was hurrying from the train at Oldham to a football match, a mile distant from the station. As he approached the football field he was seized with pain across the middle of the chest, but as it was not severe he pushed on till he arrived at the field. He sat down, but the pain increased, striking into both arms, and his hands went white and cold. He felt as if he wanted to breathe deeply but could not. He endured the suffering for twenty minutes, and as it became worse, and he felt as if he would die, he was assisted off the field, put into a cab and driven to the station. He was given some brandy which made him sick. The pain gradually diminished, and he returned to Burnley by train; as he was better he walked home (about a quarter of a mile), but felt sick and short of breath. He went to bed, and one of my colleagues saw him and found his pulse between 30 and 40 beats per minute. I saw him next morning. He felt very weak; the pain was nearly gone, though it had kept recurring through the night.

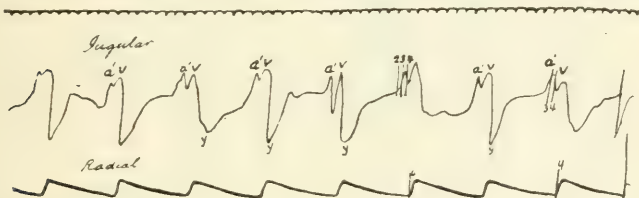


Fig. 4. Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular form; the wave *a'* occurring during ventricular systole. Pulse rate 40 per minute. (T.A., 24th November, 1907.)

He had some pain if he took a deep breath. The pulse rate was 52, the heart's dulness extended from mid-sternum to 2 inches beyond the nipple line;

apex beat faint in the 5th interspace; sounds clear and free from murmur. The superficial jugular vein was very full but did not pulsate. The deep jugular was large, filling up during ventricular systole, and collapsing suddenly at the beginning of ventricular diastole (Fig. 4). There was no sign of an auricular wave preceding the ventricular systole. The patient was kept in bed, and his condition did not undergo much change for the next fortnight, except that the pain gradually grew less till it finally disappeared and he was able to sit up. The pulse rate varied, sometimes falling as low as 30, but never rising above 52. On the 24th November a long tracing

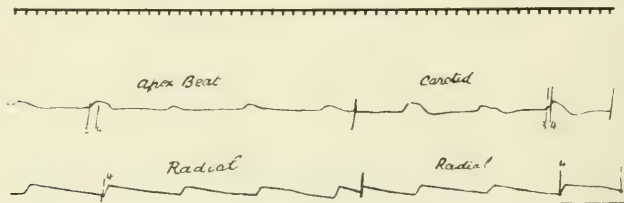


Fig. 5. Simultaneous tracings of the apex beat and radial pulse in the first part of the tracing, and of the carotid and radial in the latter part, to show the apex-radial interval (space between the lines 2 and 4), and the carotid-radial interval (space between 3 and 4) to assist in the interpretation of Figs. 4 and 6.

was taken with the ink polygraph, and the rate showed great uniformity; the rhythm was also quite regular. Figs. 4 and 6 are small portions of the tracing taken on that day, and represent the same features as were present on the 10th November; the rate was 40 per minute, the rhythm regular, and the venous pulse of the ventricular form. When I next examined him on the 29th November, his pulse had increased in rate, with occasional intermissions, shown in the radial tracings of Fig. 7. I had now the greatest difficulty in getting a tracing of the jugular pulse; he had a very short fat neck. But imperfect as the tracings are they show a return of the auricular wave *a* to its normal period before *c*. The record of the jugular pulse is not sufficiently clear to enable me to recognise with certainty the cause of the intermissions, the difference in their length probably indicates a difference in their cause. From this date he gradually improved, and has been able to get about, though he is perhaps a little shorter of breath than before his attack. I took tracings from him in December, 1908, and Dr. John Watson took the tracing (Figs. 8 and 8a) on the 11th May, 1909. The venous pulse was the same on both occasions, and showed an auricular wave, *a*, preceding the carotid wave, *c*, while the rate was 68 per minute; the rhythm was regular as in Figs. 8 and 8a.

The tracings of the jugular pulse in Figs. 4 and 6 show a variation in their character during the ventricular systole, the wave is sometimes split in two. This division varies with the respiration, and is greatest during inspiration,

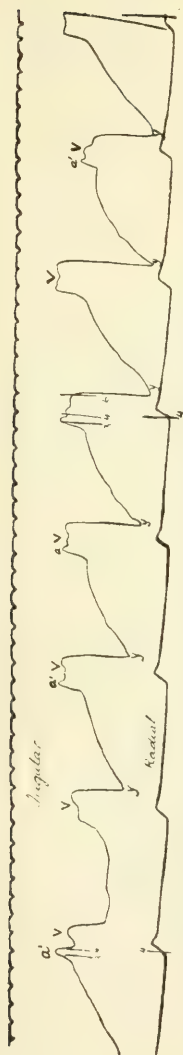
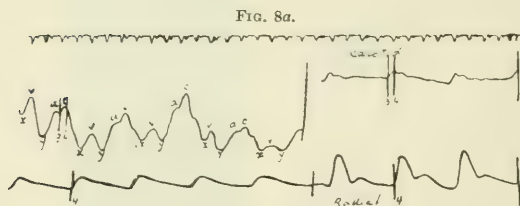
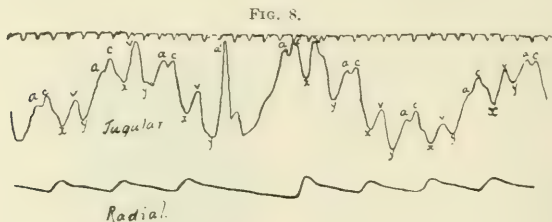


Fig. 6. Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular form, and shows the wave a' preceding by a short interval the time of the carotid pulse (perpendicular line 3). The paper was travelling at a quicker rate than when Figs. 5 and 6 were taken, as shown by the wider interval in the time marks. Pulse rate 40 per minute. (T.A., 24th November, 1907.)



Fig. 7. The jugular tracing was difficult to record, but it shows the return of the auricle to the normal period in the cardiac cycle. Intermittences of the radial were frequent, and of variable duration, but the jugular pulse is not clear enough to afford evidence of their nature. Pulse rate 74 per minute. (T.A., 29th November, 1907.)

while it almost disappears when the breath is held, the vein becoming full and turgid as in the latter part of Fig. 6. When an accurate analysis of the time of the appearance of the wave a' is made, it is found to precede the time of appearance of the carotid pulse, but to be synchronous with the beginning



Figs. 8 and 8a. (Fig. 8a is the direct continuation of Fig. 8.) Simultaneous tracings of the jugular and radial pulses in the first part of this tracing, and of the carotid and radial in the last part. The rate is 72 per minute, and the rhythm regular except for an occasional intermission which the jugular tracing shows to be due to a ventricular extrasystole—the large wave, a' , being due to the normal auricular systole occurring at the same time as the premature ventricular contraction, so that the blood from the auricle cannot enter into the ventricle, and is, therefore, thrown back into the veins, producing the large wave a' . (T.A., 11th May, 1909.)

of ventricular systole. Thus Fig. 5 shows the apex beat and radial pulse, and the interval between the perpendicular lines 2 and 4 gives the time between the beginning of ventricular systole and the appearance of the pulse in the radial. In Fig. 4 the same interval between 2 and 4 is shown to exist between the appearance of the wave a' and the radial pulse, while the time between 3 and 4 represents the carotid-radial interval as shown in Fig. 5. From these tracings it can be stated that the factor producing the wave a' coincided with the beginning of ventricular systole, and, as I shall show, there is presumptive evidence that the wave a' was caused by the auricular systole.

Case 3.—Inception of the nodal rhythm, the heart's rate at first not infrequent, but becoming slow with attacks of unconsciousness and epileptic fits. Recovery from these attacks with an increase in the heart's rate.

Male, born 1838. I have known this patient intimately since 1894. He was a healthy, vigorous man up till 1907. He was a very heavy smoker, and for a great many years he smoked two ounces of tobacco and half a dozen cigars a day. I had occasion to examine him in 1906, and found his heart normal in rate and rhythm, though for some years he had been rather short of breath. I again examined him in February, 1907, and found that his heart was continuously irregular with the disorderly rhythm characteristic of the nodal rhythm (Figs. 11 and 12). He was not conscious of the change, but there was a further increase in his breathlessness. He was still able to attend

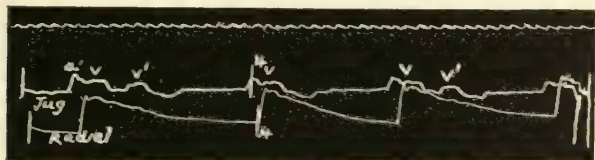


Fig. 9. 'Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular form. During the long pauses in the radial pulse, there are small premature beats, *v'*, in the jugular. The pulse rate varied from 25 to 30 beats per minute. The patient was just recovering from a series of syncopal and epileptic attacks. (W.N., 11th October, 1907.)

to business, and to play a game of golf. He lived some distance from me, and I did not see him again until the 11th October, 1907, when I was asked to see him with his medical attendant, Dr. O'Connor, to whom I am indebted for an excellent account of his many seizures. The history given was that his pulse had become very slow for some months, and that latterly

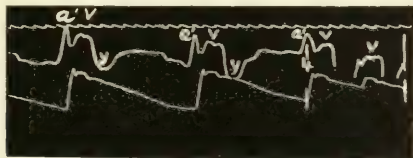


Fig. 10 shows the same features as in Fig. 9, except the wave *a'* and fall *y* is more distinct. (W.N., 11th October, 1907.)

he had been seized at times with attacks of unconsciousness. The pulse rate on such occasions was found below 30 beats per minute. He was very weak and faint when I saw him, the pulse varying in rate from 30 to 40 beats per minute, and irregular with long pauses at times. During the long pauses

there was often a small premature beat in the jugular (see *v'* Fig. 9). The heart's dulness extended $1\frac{1}{2}$ inches beyond the left nipple, and there was a soft blowing murmur at the apex. There was a small amount of albumen in the urine. The attacks of unconsciousness continued, and I saw him again in November, when the heart's condition was much the same. After this the pulse rate increased, the attacks disappeared, and he went to Torquay in June, 1908, where he had a slight recurrence of his attacks of loss of consciousness. From this he recovered, and continued well till the 4th August, when after some effort he was seized with great breathlessness, and the attacks of unconsciousness recurred. These increased in number and severity, and for two whole days he was unconscious and deeply cyanosed. For some hours he passed from one epileptic seizure to another as if affected with uræmic convulsions. He also developed Cheyne-Stokes respiration. The pulse during these convulsive attacks was not perceptible. The severity of the attacks gradually lessened, and in the month of September his pulse rate rose to 50 or 60 beats per minute. In October he had a number of very transient fainting attacks. Dr. O'Connor described the attacks as resembling *petit-mal*. Thus, while the doctor was talking to him, the patient's face would suddenly become pale, and consciousness would be lost for a brief period. During these attacks no pulse could be felt at the radial.

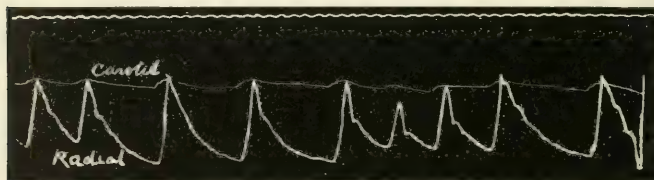


Fig. 11. Simultaneous tracings of the carotid and radial pulses. The patient had been free from syncopal attacks for some months, and the pulse rate was usually between 60 and 70. There was no jugular pulse, and the only movement recorded in the neck was due to the carotid. (W.N., 18th December, 1908.)

I saw him again on the 18th December, 1908. He was able to go about, and had been free from attacks for a few weeks. The pulse was rather slow, about 60 per minute, and irregular (Fig. 11). The heart's dulness extended $1\frac{1}{2}$ inches beyond the left nipple, the sounds were clear, with a faint doubling of the first sound. There was no pulsation in the veins of the neck, and the movement registered in Fig. 11 was entirely due to the carotid. There was no drowsy, and the urine was free from albumen.

On the 5th May, 1909, he was seen by Dr. John Hay, who took a long tracing with the ink polygraph. The rhythm was of the disorderly kind, characteristic of the nodal rhythm, and the jugular pulse was of the ventricular form. I had looked upon this case, at first, as an instance of Adams-Stokes

syndrome, due to heart-block, but at the time I was puzzled to account for the fact that he had nodal rhythm prior to the onset of the attacks of

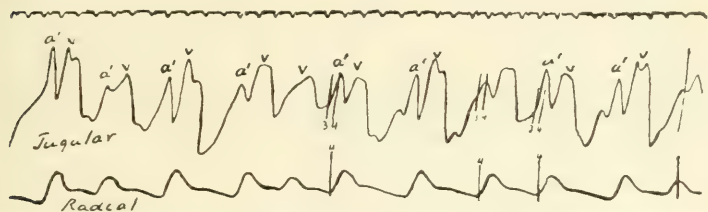


Fig. 12. Simultaneous tracings of the jugular and radial pulses. The rhythm is disorderly, and the jugular pulse of the ventricular form. (W.N., 5th May, 1909.)

unconsciousness and slow heart rate, and also because of the nature of the jugular pulse in Figs. 9 and 10, where it is shown to be of the ventricular type. The tracing of the jugular has never been shown to be of this type in cases of heart-block. Case 2, which came under my observation in December, 1907, also puzzled me, and it was only when I began to analyse the tracings more carefully that the nature of the tracings from this patient dawned upon me, and that it became obvious that here we had an instance not of blocking of the stimulus between auricle and ventricle, but one of slow nodal rhythm producing anæmia of the brain.

Case 4.—Permanent nodal rhythm, bradycardia associated with mitral stenosis. Occasional attacks of syncope and convulsions (Adams-Stokes syndrome).

(I am indebted to Dr. Gordon Goodhardt for the opportunity of examining this patient.)

Male, born 1865. When a soldier in India he had dysentery at the age of 20, syphilis at the age of 22. He had malarial fever in America at the age of 27. In 1894 he had the first attack of syncope. After lying up a week he went out, and in hurrying to avoid a cab he fell unconscious on the pavement, but quickly recovered. He consulted a doctor, who said his heart was affected. Two years later he was laid up with shortness of breath and swelling of the legs, and was treated for "mitral disease." He partially recovered, and had frequent attacks of weakness until the final breakdown occurred in 1905. He had been feeling ill for some years, but had worked hard, and had kept himself going on brandy, bovril, eggs, etc. He says his pulse was slow four years ago, and that it has remained so ever since.

In 1904 he began to have mild "fits" in which he lost consciousness and was slightly convulsed. From November, 1905, to April, 1906, he had a great number of fits, some severe with convulsions and cyanosis, others slight without convulsions. He had no attacks for a year, but he had a very

severe one in April, 1907, and since then only three mild attacks. He had lived a life of hard work with frequent bouts of drinking.

The patient is tall, spare, and intelligent looking. The face is usually ruddy, with a faint duskiness. He walks slowly and carefully, and his gait is slightly ataxic; if he hurries or gets excited he becomes giddy. He has a somewhat violent temper, and when in a passion his face becomes dusky and cyanosed. When lying down there is a large pulsation, seen in the deep jugular on both sides, heaving in the lower part of the neck, as in Fig. 13, more abrupt and divided into two at the upper part, as in Figs. 14 and 15. It is very slow and synchronous with the apex beat.

The radial pulse is slow and deliberate, usually about 30 per minute.

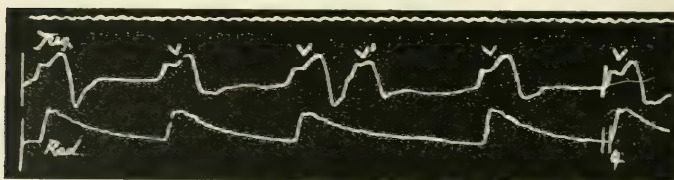


Fig. 13. Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular form, and the rate about 28 per minute. (M.M., 9th November, 1908.)

At times two beats are close together, and are followed by a long pause. These coupled beats may appear at rare intervals or alternate with a single beat, or they may appear continuously for a short period. The apex beat is large and diffuse in the 6th interspace, and in the anterior axillary line. The heart dulness extends 1 inch to the right of the middle line and 8 inches to the left.

There is a rough blowing systolic murmur heard best at the apex and propagated towards the axilla. The second sound is clear and well struck and followed by a soft murmur. This diastolic murmur is heard only over a limited space at the apex, and is not always perceptible. It is, as a rule, faint and fades away. (The sounds and murmurs as heard at the apex are diagrammatically drawn in Fig. 14).

A large number of tracings have been taken from this patient at different times and they always present the same features, the only difference being that sometimes the coupled beats, as in Fig. 13, are more frequent or are entirely absent. The rhythm is, as a rule, quite regular though an irregularity like that shown in Fig. 14 may sometimes be detected. The jugular tracing shows one large wave occupying the whole time of ventricular systole. The beginning is synchronous with the carotid pulse as in Fig. 15. In some tracings taken about the middle of the neck, the

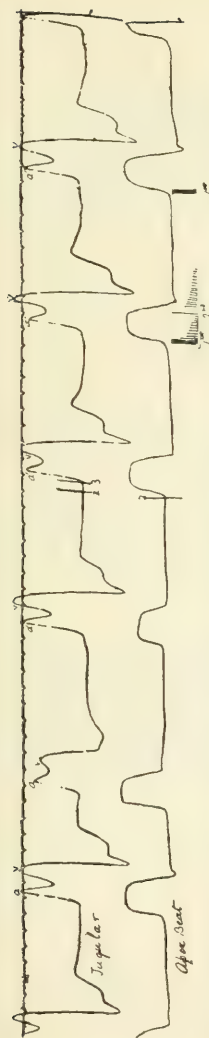


Fig. 14. Simultaneous tracings of the jugular and apex beat. The jugular tracings show two waves, a' and v , occurring during ventricular systole. The heart rate is about 32 per minute. The down strokes and shading represent the 1st and 2nd sounds and the position of the murmurs heard at the apex. (M.M. 27th April, 1909.)

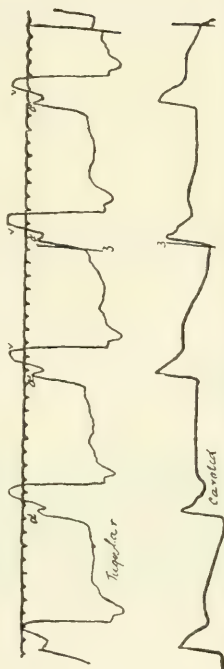


Fig. 15. Simultaneous tracings of jugular and carotid pulses, showing their synchronous occurrence. (M.M., 29th April, 1909.)

wave is divided: the first part I have marked *a'*. Though synchronous with the carotid it is not due to the carotid as its presence is quite perceptible in the vein. The later of the coupled beats may not be present in the radial, but is always distinct in the jugular and apex tracings.

The presence of systolic and diastolic murmurs at the apex indicates a lesion of the mitral valves. The diastolic murmur also indicates that there is a certain degree of stenosis, and here, as in other forms of nodal rhythm, there is a complete absence of an auricular-systolic (presystolic) murmur preceding the first sound.

III. THE TENDENCY TO STAND-STILL OF THE HEART IN NODAL RHYTHM, WITH NOTES OF TWO FURTHER CASES.

The tendency for long pauses in the heart's action in cases of nodal rhythm, such as those seen in Figs. 2 and 9, has been a matter of interest to me for many years. These pauses may not produce any symptoms, but they may last long enough to produce anæmia of the brain with transient loss of consciousness, and even the more prominent phenomena of Adams-Stokes syndrome (cases 3 and 4). The symptoms then resemble those of the more common condition, auriculo-ventricular block. I have been impressed by the fact that not a few cases of nodal rhythm die suddenly, and it seems that this tendency to long pauses shown in the figures may be the immediate cause of death, as in case 5. The proof of this view is not complete, but the following cases are also very suggestive.

Case 5.—Nodal rhythm, with long pauses in the heart's action, producing attacks of unconsciousness and probably the death of the patient.

Female, born 1854. I had known this lady for many years. She had a large goitre, and for the last few years of her life her heart was continuously irregular. She was not robust, but was able to attend to her household duties; she was liable to attacks of palpitation, and had frequent attacks of syncope, which I could not account for at that time. On the 2nd July, 1902, I was summoned to see her, and on my arrival I found her recovering from an attack of unconsciousness during which she had been convulsed. Her face had a deathly ex-sanguine appearance. She gradually recovered, and her colour improved in the course of half an hour. On inquiry, I found that she was talking to her sister when she fell down in a faint and became convulsed for a few minutes.

When I examined her, the heart was acting irregularly but with fair strength. During the next few days her heart was irregular with long pauses as shown in Fig. 16, taken on the 3rd July, 1902. She sometimes lost consciousness for a few seconds, but I did not see her at those times. On the

7th July I was again summoned to see her, but when I arrived she was dead. I was informed that she had again fainted, become convulsed, and then lay quite quiet.

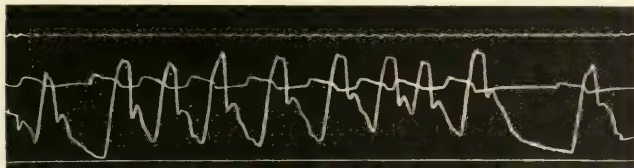


Fig. 16. Simultaneous tracings of the apex-beat, and of the radial pulse. The rhythm is disorderly and characteristic of the nodal rhythm, with frequent long pauses. It was probably in consequence of these long pauses that the patient suffered from attacks of unconsciousness and convulsions. (M.B., 7th July, 1902.)

Case 6.—Large auricular waves in the jugular and liver pulses. Presystolic mitral and tricuspid murmurs. Sudden disappearance of all signs of auricular contraction with the appearance of the nodal rhythm. Sudden death.

This case is recorded in more detail elsewhere¹.

Female, born 1862. This patient had been under my care for a few years, and amongst other phenomena there were mitral and tricuspid presystolic murmurs, large pulsation of the jugular bulb, the big wave was visible at a distance of many yards, and the patient was conscious of the pulsation

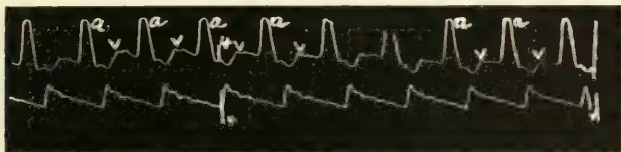


Fig. 17. Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the auricular form, there being a large wave, *a*, due to the auricular systole. There were also present tricuspid and mitral presystolic murmurs, and an auricular liver pulse. (A.R., 4th October, 1895.)

in the jugular bulb. The time of its appearance showed it to be due to the auricular systole (Fig. 17). The pulsation did not extend into the jugular veins in the neck, as the valves above the bulb were competent, and closed with such force that a short sharp sound was produced, which was synchronous with the large wave, and preceded the first sound of the heart. There was also a marked pulsation in the liver due to the auricular systole.

The heart was invariably regular, except on one or two occasions, when I detected an extrasystole. On the 9th October, 1895, she called my attention to the fact that the beating in the neck had ceased during the previous night. On examination I found that the heart was irregular, with a tendency to long pauses, that the auricular wave had gone from the jugular bulb (Fig. 18),

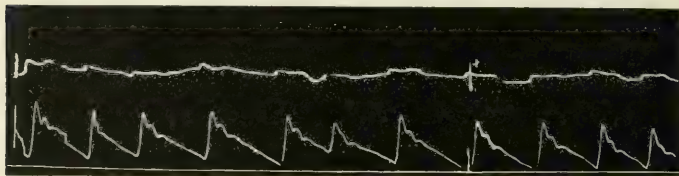


Fig. 18. The upper tracing was taken from the neck at the place from which the jugular pulse in Fig. 17 was taken a week later. There is no auricular wave present, and only one small wave during ventricular systole. The rhythm is irregular, and slower than in Fig. 19; the presystolic murmurs and the liver pulse had disappeared. The patient fell down and died three days after the inception of this abnormal rhythm. (A.R., 12th October, 1895.)

and that there was no pulsation in the liver. The presystolic murmurs at the mitral and tricuspid orifices had disappeared, and also the auricular sound in the jugular bulb.

On the 13th October, 1895, on getting out of bed, she fell down and died.

IV. THE ACTION OF THE AURICLE IN NODAL RHYTHM.

From the study of the foregoing cases it can be seen that there is a slow action of the heart, which is coincident with the disappearance of the auricular systole from the normal period in the cardiac cycle. The question arises. What is the auricle doing?

In my earlier observations I had watched individual cases, and had seen the ventricular wave, *v*, of the auricular venous pulse gradually increase in size, till finally the venous pulse changed from the auricular form. From this I inferred that the auricle had become so engorged that it ceased to contract. Some support for this view was found in the great distension of the auricles and thinning of the auricular wall, which I found post mortem in a patient in whom I had detected these changes during life. Further observation showed that this experience was exceptional; that in many patients the appearance of the ventricular venous pulse was sudden and not produced by a gradual increase in size of the *v* wave, while there were other patients who exhibited the ventricular venous pulse for many years, and a hypertrophied auricular muscle was found post mortem. It was impossible to

conceive that such hypertrophied muscle could have been inactive for years. Further, in a number of cases the nodal rhythm was transient—the auricle suddenly appearing in its normal place, and the heart reverting to its normal action. A more careful inspection of the jugular veins during life revealed the fact that during the systole of the ventricles two waves could be seen, which could be shown in the tracings, one wave short and abrupt, synchronous with

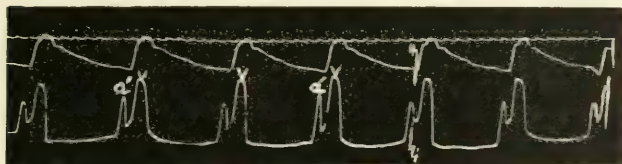


Fig. 19. Simultaneous tracings of the radial and jugular pulses. The jugular tracing is of the ventricular type, and shows a well-marked wave, a' , due probably to the auricle contracting at the same time as the ventricle. Rate 38 per minute. The infrequent rate is due to digitalis.

the beginning of the ventricular systole (a' Fig. 19), and the other slower and larger, lasting during the remainder of systole (v Fig. 19). I reasoned from such instances that the auricle must have contracted during the ventricular systole, that the fall after a' in such a tracing as in Fig. 19 was really due to the diastole of the auricle. This view was strengthened by the fact that occasionally, when the ventricle paused, the wave a' would appear by itself, and was not followed by the wave v , as I have described elsewhere⁵. In carefully examining a large number of cases I found the wave a' exactly synchronous with the beginning of the carotid pulse, as in Figs. 3 and 15, and careful inspection in suitable cases showed that it was not due to the carotid but to an actual wave in the veins. I reasoned that in such cases the ventricle must have begun to contract before the auricle, inasmuch as there is a slight delay (the presphygmie interval) between the beginning of the ventricular systole and the appearance of the carotid pulse, and, therefore, in these cases, between the beginning of the ventricular systole and the auricular systole. In a few cases I found that this delay was absent, and that the wave a' preceded the carotid pulse by a brief interval, as in Fig. 6.

Recently, abnormal rhythms of the heart have been produced experimentally (cp. Cushny, this *Journal*, page 1)*. They include a rapid action of the heart with ventricle and auricle contracting simultaneously, the ventricular systole preceding the auricular by a brief interval, and also a slow action of the heart with ventricle and auricle contracting simultaneously, the

* Similar results, as yet unpublished, have been obtained by Biggs and Lewis.

ventricle usually preceding the auricular contraction, but sometimes auricle and ventricle starting simultaneously.

V. PHYSIOLOGICAL AND PATHOLOGICAL CONSIDERATIONS.

From a study of these cases we must conclude that there are regions in the heart capable of starting and maintaining a rhythm other than that of the normal rhythmic area. Assuming that the view of simultaneous contraction of auricle and ventricle is correct, there must be such an area situated in some region where the stimulus can reach the auricle and ventricle at the same moment, or where the ventricle receives the stimulus before the auricle. When we consider that the starting of the heart's contraction is normally in tissue which represents in the mammalian heart the sinus venosus of the lower animals, it may be surmised that these abnormal starting places will be in primitive tissues of the same origin as the remains of the sinus venosus. We now recognise that the auriculo-ventricular node and bundle are the remains of the primitive cardiac tube, and as the node appears to be suitably situated, I have suggested that this may be the place.

I had reasoned that as the heart's contraction starts at the most excitable place, it was probable that the node or the bundle in its neighbourhood was made more excitable than the normal rhythmic area by some morbid process invading it. In order to test this view I collected the hearts of a number of patients, who had shown the abnormal rhythm during life, and sent them for examination to Dr. Arthur Keith.

In these hearts Dr. Keith found that the node and bundle were invaded by cicatricial tissue, or by inflammatory cells. In these instances the morbid process was but part of a similar condition affecting the adjacent muscular tissue, so that one could not draw the conclusion that the abnormal rhythm was due alone to irritation of the node with certainty, although the condition afforded presumptive evidence in favour of such a view.

With one exception all these cases had shown at one time or other an increased rate, during life. Sometimes the rate was greatly increased and intermittent (paroxysmal tachycardia), and it could be reasoned that the node, being more excitable, started the contraction before the normal rhythmic area. How is this slow nodal rhythm to be accounted for? From a study of these cases it is not only obvious that slow nodal rhythm may arise without any previous increase in the heart's rate, but, as in case 3, a fast nodal rhythm of the usual form may be succeeded by a slow one. One must, therefore, conclude that an area in the region between auricle and ventricle exists which is capable of inducing a slow cardiac rhythm of this abnormal type, and that the disease in its progress has invaded and stimulated this area.

MacWilliam⁹ described a small area in the auricular wall, near the coronary sinus, stimulation of which invariably produced marked slowing of the ventricular rate. It is quite conceivable that the disease occurring in this

neighbourhood may have extended to and affected the inhibitory area of MacWilliam, or some other similar region. In certain cases of nodal rhythm with a frequent heart rate, a slow nodal rhythm can be induced by the action of digitalis (Fig. 19). So sensitive are certain of these nodal rhythm hearts to digitalis that I have been able to increase or to diminish the heart rate by exhibiting or withholding the drug.

This form of slow ventricular and auricular action is quite distinct from heart-block, to which otherwise it has certain affinities. In the latter condition there is an interruption of the stimulus between auricle and ventricle, so that the ventricle does not respond to all the auricular systoles, or, if the block is complete, the ventricle pursues an independent rhythm of its own. In such conditions, if a venous pulse is present, it always shows waves due to the auricular systole, and a jugular pulse of the ventricular type is never seen. But that there is some close relationship between heart-block and the nodal rhythm is evident from the history of case 1, where the increased *a-c* interval, and the partial heart-block from which he suffered in 1897, shows that the lesion had invaded the auriculo-ventricular bundle. However, when the bradycardia appeared it could be proved not to have resulted from an increase in the heart-block, for there was a total absence of all signs of auricular action during ventricular diastole, and the venous pulse was of the ventricular type. Slight heart-block is of frequent occurrence in cases of mitral disease after rheumatic fever, and even complete heart-block may occur in rheumatic heart affection, as shown in a case recorded by Bramwell¹.

The resemblance of complete heart-block, in man, to the results obtained by destroying the connection between the auricle and ventricle in a frog's heart (second Stannius ligature) has long been recognised. After such an experiment the sinus and the auricle continue beating at the normal rate, while after a pause, more or less prolonged, the ventricle beats at a slower rate and with an independent rhythm.

Engelmann², by placing a ligature between the sinus and auricle of a frog's heart, so carefully that no portion of the sinus structure was left on the auricular side of the ligature, obtained a response in which auricle and ventricle contracted independently of the sinus. The response was of such a nature that both chambers contracted synchronously, the ventricular often slightly preceding the auricular systole; a result corresponding to that, which I have pointed out as occurring in nodal rhythm. Wenckebach⁷ suggested that the nodal rhythm was of a nature similar to that obtained by Engelmann by the first Stannius ligature. I think that the more common form of nodal rhythm, when the rate is greater than normal, is explicable only on the hypothesis of an irritation rendering the node or adjacent part more excitable. The slow form of nodal rhythm described in this article has a very close affinity to the rhythm produced in Engelmann's experiment, and one might be disposed to speak of this form of it as a "sino-auricular block." But there is a difficulty in regard to the mammalian heart, inasmuch as the sinus is not a distinct structure; in the course of development it

has become absorbed to form parts of the superior vena cava wall, of the right auricle and of the coronary sinus, and it is scarcely conceivable that a structure so widely distributed would have all its connections with the auricle disturbed.

CONCLUSIONS.

1. The heart's action may start continuously from a place other than the normal starting place, and in the resultant rhythm the auricular systole no longer precedes the ventricular. This abnormal rhythm is provisionally called "nodal rhythm."

2. The rate of the "nodal rhythm" is usually more frequent than the normal rate.

3. In this paper a form of nodal rhythm of infrequent rate is described. This form of bradycardia may arise suddenly in a heart previously showing the normal rhythm, or it may arise in a heart previously showing the nodal rhythm with a rate more frequent than the normal. It may be quite regular or may show premature beats, or it may be continuously irregular with a tendency to long pauses. While related to the more common forms of nodal rhythm, it may occur in a patient with slight heart-block (cp. case 1).

BIBLIOGRAPHY.

- ¹ BRAMWELL. B.M.J., 1900, i, 995.
- ² ENGELMANN. Archiv f. Anat. u. Physiol., 1903, Phys. Abth., 505.
- ³ MACKENZIE. "Diseases of the Heart," London, p. 324.
- ⁴ MACKENZIE. Edin. Hosp. Reports, 1898, v, 22.
- ⁵ MACKENZIE. B.M.J., 1904, i, 532, Fig. 17.
- ⁶ MACWILLIAM. Journ. of Physiol., 1888, ix, 380.
- ⁷ WENCKEBACH. Archiv. f. Anat. u. Physiol., 1907, Phys. Abth., 18.

PAROXYSMAL TACHYCARDIA.

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SINCE 1867, in which year Cotton³ wrote of a case of "unusually rapid action of the heart," numbers of cases of a similar nature have been carefully observed and recorded. Herringham, in 1897, was able to collect forty examples of "paroxysmal tachycardia,"¹⁰ and the symptomatology has been dealt with at length by him and by previous and subsequent writers. But a new stage has now been reached at which we are forced to admit that more than one type of case has been included in this category. We know that there are at least two definite and distinct forms of the affection, and in the future they will require separate consideration. There is a form in which the venous pulse is of the ventricular type, and in which there is reason to believe that the auricles fail to contract at the usual instant in the cardiac cycle. There is a second type in which the auricular form of venous pulse is present.

It is consequently necessary, for the elucidation of the pathology of these conditions, that they should receive further and individual attention, and that the symptom groups associated with each should be carefully observed. It is an unfortunate fact that, while a great deal of labour has been expended in collecting the essential data, the work has to be largely revised; for although we are acquainted with many of the etiological factors of paroxysmal tachycardia as a whole, as yet we cannot allocate the separate factors to their respective groups, neither are we at present sufficiently conversant with the peculiar symptomatology of either form. Previous observations are, however, invaluable in directing the course of observation. Moreover, it is probable that the two forms of the disease or syndrome have much in common. Thus, in so far as the clinical picture depends directly upon accelerated action of the ventricles, so far will they be found to correspond. It is also probable that eventually the two types may be found to have a parallel pathology, for each obviously depends upon an exaggerated rate of stimulus production. It is reasonable to assume that the essential difference between the two conditions lies in the level of the heart at which the morbid process arises or first develops to the critical point.

The present observations will be confined in the main to a detailed examination of a single case of that form of paroxysmal tachycardia, in which the auricle is responsible for the ventricular beat, for as yet no such case has been fully recorded, and far less is known of this condition than of the

sister affection, the "ventricular" or "nodal" type*. References to previous observations will be few, for in the present state of our knowledge it is imperative that confusion between one type and the other should be diligently avoided, and a discussion of the vast majority of previously reported cases, and an attempt to place them in their respective groups would, in the absence of records of the right auricular movements, be more speculative than profitable.

Two cases of paroxysmal tachycardia were reported by Schmoll²¹, and one of them certainly, and the other probably, belonged to the auricular group. In the previous year Hirschfelder reported a case¹¹ and though interpreted as the ventricular form, some doubt may be felt as to whether it does not in reality belong to the auricular type. Hay's case⁹ (No. 2) belongs to the auricular type, though here again the author interprets his tracings differently. A careful comparison of the curves given in this communication with those of Hay, will speedily lead to the conclusion that they are of the same nature. Lastly, an undoubted and recognised case has been briefly described by Cowan, McDonald, and Binning⁴.

Before proceeding to the main subject matter of this paper the writer desires to express his gratitude to his colleague, Dr. Clive Riviere, who has so generously placed the case at his disposal, and to Dr. Rose Bradford, in whose wards many of the contained observations were made.

I. A CASE OF PAROXYSMAL TACHYCARDIA OF THE AURICULAR TYPE.—CASE I.

(A.) *History, etc.*

J.A., a labourer, aged 67, was first admitted to the out-patient department at the City of London Hospital on the 1st October, 1908.

Family history. His father died, aged 68, "of some complaint like" his own; he used to have giddy attacks†. The mother died young, and the cause is unknown. Several brothers and sisters are living, but the patient knows nothing of them. He has eight children, all of whom are healthy, and has lost one child, of convulsions. There is no history of family affection. *Past history and habits.*—The patient has always enjoyed good health, and has suffered from no previous ailment. Rheumatic fever and syphilis are denied. His work has been heavy, and at times there have been slight pains in the limbs subsequent to a hard day's work. He has partaken of alcohol to a very moderate extent, and has always been a non-smoker. *Present affection.*—Six

* Those interested in the "ventricular" or "nodal" form may consult Mackenzie¹⁴.

† It is often stated that paroxysmal tachycardia may be hereditary. In Oettinger's case¹⁷ attacks of palpitation were recorded in several of the ancestors. In Williams' case²² the "mother had suffered from similar attacks." In these instances the evidence is entirely insufficient. Falconer⁷ has recorded paroxysmal tachycardia in a mother and daughter, in both of whom a valvular lesion was present. The nodal form of periodic tachycardia is not uncommon in rheumatic heart affection, and it is the hereditary tendency of such heart affection, and not that of the tachycardia *per se* which should command attention. Similarly, in Faisan's case⁶, where mother and daughter were affected, there was family albuminuria and malarial infection.

years ago the patient suffered from transient attacks of giddiness. At times there were several in one day, but often a month elapsed between consecutive attacks. A little more than two years ago he was disturbed by attacks of *uneasiness* at the pit of the stomach. Sometimes they followed his meals, and they were usually aggravated by the ingestion of food. Often they were brought on by exercise. Later he noted *breathlessness*, usually associated with the abdominal symptoms, but frequently occurring in their absence. It was increased by exertion. For eighteen months he has recognised the grouped nature of his symptoms, which he now terms "attacks," but he has until recently been unaware of the accompanying increase of pulse rate. He states that *he has always been aware when an attack threatened**, by a feeling of slight weight or dull aching *pain* in the lower part of the chest or pit of the stomach. The attacks themselves have consisted of an intensification of these symptoms, often associated with other subjective manifestations. *Palpitation* has been present at times, and is described as a fluttering feeling over the precordium and upper abdomen. It has never been prominent. Often he has experienced a "strange sensation, like wind, passing up the middle of the chest," and the latter might rise to his throat and be accompanied by a sensation of *constriction*." The sensation would partly remain in the throat, and partly extend to the head, and a dull aching pain in the head might be superadded. When present, the headache generally persisted until some time after the termination of the attack. The curious sensation in the head was always momentary, "rarely lasting more than a few seconds." It was accompanied by *giddiness* and transient "*loss of memory*." In more severe attacks the onset was rapid, the sensation mounting instantly to the head, and the patient "felt things swimming round," and fell down. There was occasional *loss of consciousness*, usually brief, sometimes lasting a minute or two. Such disturbances were in the main confined to the earlier days of the illness, and he has never been subject to any further epileptic manifestations. Return to consciousness is described as resembling awakening from sleep, but he has often been "shaky" though never actually trembling at such times. Soreness of the elbow, and a curious numb feeling in the *radial* side of the left forearm have been present on occasion, but have not necessarily been associated with an attack. *Flatulence* has been a prominent symptom, and is regarded as frequently heralding attacks, while the passage of flatus has often given relief. During the past twelve months work has been abandoned of necessity.

(B.) *The physical signs when the heart beats slow.*

The patient is a well-built man of good colour. He has an easily reducible left inguinal hernia of many years standing, and an old united fracture of the left tibia. In the neck, just above the inner ends of the clavicles, are two tumours about the size of pigeon eggs, placed symmetrically and freely movable under the skin. They are probably of a fatty nature, and appear to have no relationship to the remaining condition. *The chest and lungs*.—The chest is barrel shaped and rigid; respiratory movement is limited. The percussion note is moderate, and the superficial cardiac dulness is reduced. Auscultation reveals distant breath sounds and frequent sonorous rhonchi over the bases and axillæ. *The heart*.—The H.A.B. is indistinct, but the shock can be identified internal to the nipple line. The deep limits of cardiac dulness are as follows: R.L. mid-sternal line; L.L. $3\frac{1}{2}$ inches from mid-sternal line. U.L. fourth rib. The left limit moves three-quarters of an inch on rolling from side to side†. The heart sounds are normal, but a little distant. There are no murmurs. *The arteries*.—There is a considerable degree of arterio-sclerosis. The pulse is of moderate tension; the rate is

* This has in reality resulted from his inability to recognise the immediate onset of the attacks, as will be shown in the sequel.

† In Hoffmann's series¹² a remarkable movement of the heart with posture was found, and some stress was laid upon the observation.

within normal limits ; there are occasional irregularities (cp. description of Figs. 2 and 3). *The urine*.—Sp. Gr. 1010 to 1020. Quantity normal. No albumen or sugar. *The nervous system and abdomen*.—Nothing abnormal found.

(c.) *Physical signs connected with the paroxysms.*

The attacks are invariably absolutely abrupt in onset, and terminate with equal suddenness (cp. Figs. 6 and 7a). The pulse rate varies from 140 to 220, but these rates are actually very rare, and in the great majority of the tracings obtained the rate lies between 170 and 200. The most usual rate is 180, or thereabouts. The figures represented in the charts (Figs. 9 to 12) were taken by palpation, and can, therefore, only be regarded as approximate. The small amount of variation in frequency during a single attack is often very striking, and is well illustrated by the following example :—

Pulse rate taken every half-minute for 50 minutes (as calculated from a measured and continuous pulse tracing, taken in the middle of a paroxysm).—Patient supine, 183, 183, 187, 181, 185, 183, 182, 180, 180, 187, 183, 184, 184, 181, 185, 185, 180, 189, 181, 183, 185, 185, 188, 181, 183, 189, 185, 184, 183, 183, 183, 176, 183, ; sitting, 195 ; lying, 190, 184 ; sitting, 193, 200 ; lying, 199, 186, 180, 183, 184, 181, 180, 183 ; sitting, 185, 197 ; lying, 203, 187, 185, 185. —, 180, 181, 180, 180, 170, 192, 183, 191, 185, 190, 187, 186, 185, 185, 188, 183, 185, 185. —, 185. —, 186, 184, 184, 184, 183, 185, 183, 182, 184 ; sitting, 199 ; lying, 187, 184, 183, 184, 186, —, —, 184, 185, —, 186, 184, 183, 186.

In duration the paroxysms vary. The shortest observed has been 3 minutes, but this is quite exceptional. As a rule they last several hours, and may continue a whole day and night.

At the commencement of a paroxysm, and often after its prolonged continuation, there is well marked alternation in the force of the beats, and at times the rate is difficult to estimate in the absence of records. The heart sounds are correspondingly increased, and there is rapid pulsation of the veins of the neck. At the onset there are no further physical signs, but as the paroxysm continues the left limit of cardiac dulness moves gradually towards the axilla, until it has reached a point $4\frac{1}{2}$ to $4\frac{3}{4}$ inches from the mid-sternal line. The veins become more prominent and tense. The face shows characteristic changes, which, when the attack has lasted many hours, render its recognition easy. The facies assume a greyer colour in place of the usual pink tint. There is a *soupeçon* of cyanosis in the lips and ears. The eyelids are darker, and the whole countenance wears a strained and weary expression. On rare occasions there is a short systolic murmur at the apex. The liver has been observed to enlarge slightly, but definitely, in the longer attacks. There is never dropsy or albuminuria.

At the cessation of an attack the recovery is almost immediate ; it is often preceded or accompanied by eructation or the passage of flatus.

The colour alters, the heart diminishes rapidly in size and the veins empty. The slow pulse at this stage is almost invariably markedly irregular (cp. Fig. 3).

(D.) *Subjective sensations at the onset of paroxysms.*

For some months the patient has been under close observation, and the relationship of the symptomatology to the attacks of tachycardia has been fully substantiated. Particular care has been exercised in attempting to gauge the patient's power of recognising the onset of a paroxysm, and, as a result of numerous observations, it may be said that as a rule he is unaware of a change from the slow to the fast pulse rate, until the latter has persisted for fifteen minutes, or even longer. On the other hand the cessation of a paroxysm is readily appreciated, and is invariably accompanied by relief. And this may be the case even though the preceding paroxysm is not perceived. Thus at times the patient fails to recognise an attack until it terminates. It has been quite obvious that the subjective sensations increase gradually from the onset, and that in consequence his statement of the length of an attack is unreliable. On four occasions the actual onset of an attack has been observed, and on many occasions the patient has been interrogated within five or ten minutes of the onset. On one occasion only was the onset recognised by him. The patient had been in an attack for some hours, and during the greater part of the time continuous radial and venous curves were taken. The attack suddenly ceased, and its cessation was accompanied by relief. A few minutes later, while the apparatus was being removed, the patient stated that the attack had returned, and the pulse was once more found to be fast.

(E.) *The interpretation of curves taken during the paroxysms.*

As a general rule simultaneous radial and venous curves obtained during a paroxysm are perfectly regular. The radial curves taken with the Dudgeon sphygmograph show slight respiratory undulations. In polygraph tracings, the jugular curve is characterised by a prominent *a* wave, and also shows a small *c* wave (Figs. 1 and 1*a*). The amplitude of excursion increases during the last phases of inspiration and the first phases of expiration. The *a-c* interval is, as a rule, $\frac{1}{5}$ sec., or slightly exceeds this limit. The electrocardiogram (Fig. 5*a*) shows a well-marked P wave due to auricular contraction, and a prominent R wave corresponding to ventricular systole. The second ventricular wave, T, of the normal curve is absent. The height of the *a* wave in certain of the venous curves taken during the paroxysm is due to the increased volume of the veins and to the tendency for the auricular systole to commence before the preceding ventricular systole has terminated. For this reason its size is in marked contrast to that of the *a* wave taken during the intervals between attacks. Figs. 1 and 1*a* are exceptional in that they show marked alternation,

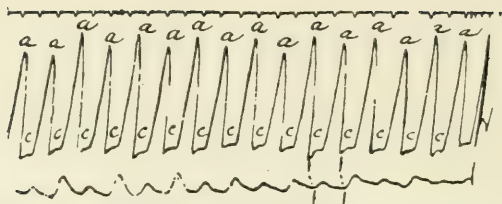


Fig. 1. Case I. Paroxysmal tachycardia. As in all similar figures the tracings show from above downwards, $\frac{1}{2}$ sec., venous pulse, radial pulse. The dotted lines joining venous and radial curves indicate corresponding points. Such points were calculated in each case from simultaneous carotid and radial curves, and the transmission distance from carotid to radial has consequently been allowed in the measurement.

The figure is an example of tracings taken during the paroxysms; pulse rate 187; respiration held; radial and venous curves show alternation, the small radial beat corresponds to the large venous beat; the venous pulse is of the auricular type.

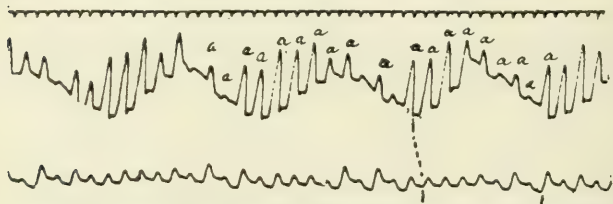


Fig. 1a. Case I. The same, during respiration. Alternation becomes very marked with each inspiration. Rate of pulse is 192.

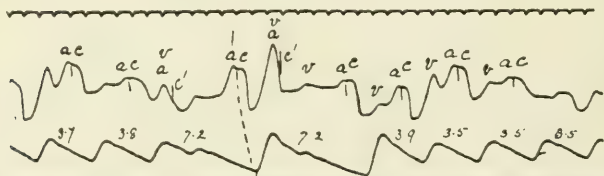


Fig. 2. $\times \frac{1}{10}$ linear. Case I. Taken between attacks. Slight sinus irregularity and two auricular extrasystoles are shown. The rate of the pulse is 82.

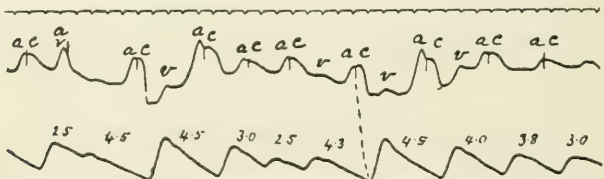
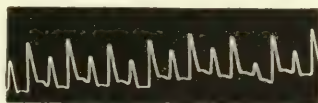


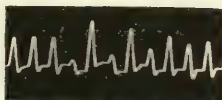
Fig. 3. $\times \frac{1}{10}$ linear. Case I. Tracing taken within ten minutes of the cessation of an attack. Auricular extrasystoles and marked sinus irregularity are present. Pulse rate about 79.

and have been specially selected on this account. In Fig. 1 alternation is also present in the jugular curve, the largest *a* waves correspond to succeeding small waves in the radial tracing. The curve was taken during a short suspension of respiration, and the venous alternation admits of a ready explanation. As stated, any given *a* wave tends to coincide in some degree with the preceding ventricular systole. In falling with a relatively inactive contraction of the ventricle, the auricular pulsation is less marked than when it coincides with a stronger ventricular beat. In many curves the absolute relationship of alternation in the venous curve to a reversed picture in the arterial tracing can be fully substantiated. In each the phenomenon commences and terminates at the same time. Moreover, the venous alternation varies in a degree corresponding to that in the arterial tracing (shown to a slight extent in Fig. 1*a*). Venous alternation in this patient is consequently attributable, not to variation in contractility in the auricle, but to the time relationships of auricular and ventricular systoles.*

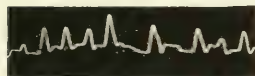
Oftentimes a striking relation occurs between alternation and respiration. Fig. 1*a* illustrates this point. As the venous curve falls, alternation in the radial pulse becomes marked, and the smaller alternate beats almost disappear. Such a relationship is often maintained over considerable



a.



b.



c.

Fig. 4*a*, *b*, and *c*. Case I. Dudgeon tracings during an attack. 4*a* shows marked alternation.

4*b* shows alternation and increased prominence of the taller waves. 4*c* shows extinction of the smaller beats as a result of alternation, and the spontaneous occurrence of a larger beat.

stretches of tracing. Dudgeon tracings of the alternation are given in Fig. 4*a*, *b*, and *c*. Fig. 4*a* shows the usual picture of alternating large and small beats occurring at equal intervals. In Fig. 4*c* alternation of a very marked character is seen. Two beats are practically ineffective. But

* Compare Cushny and Grosh⁵ (Fig. 15 and interpretation).

in both Fig. 4*b* and *c*, another phenomenon is apparent, in the form of an increased prominence of certain waves. Alternation is shown as starting either with a small or a large wave, and the succeeding wave, be it large or small, is approximately inversely proportional to the first altered wave. If alternation is to be ascribed to an affection of contractility, and there appears to be reason for the adoption of this view, then it must be acknowledged that in this instance, not only negative, but also positive inotropic (contractility) effects are present.* The extinction of beats, as shown in Fig. 4*c*, is not confined to those instances where alternation originates in an exaggerated beat, it has also been observed at the end of a long strip of alternation. Nevertheless, it is always accompanied by an increase in the size of succeeding waves. Amongst the factors which produce alternation in this patient, may be mentioned the prolongation of the paroxysm, respiration, normal or forced, coughing, or any exertion, such as the assumption of the erect posture. Alternation has also always been prominent at the commencement of attacks, a feature which must be borne in mind when the tracing showing the onset of a paroxysm is interpreted (cp. notes accompanying Fig. 12). In brief, alternation in the radial pulse is present at such times as one might be led to expect it, namely, when an extra strain is thrown upon the action of the ventricles. The electrocardiogram (Fig. 5*a*) shows regularity in the force of ventricular contraction at the time when this curve was taken.

(F.) *The interpretation of curves taken between the attacks.*

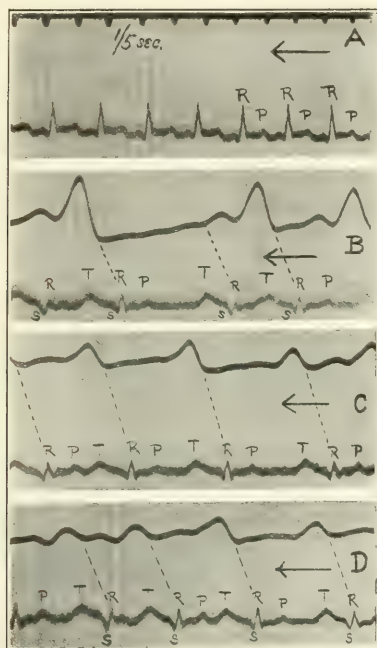
The irregularities described in this paragraph are those which occur when the pulse has been slow for a considerable period. It may be said at once that the pulse is rarely regular for many beats together. It may be once in a few beats, it may be once a minute that one or more extra beats disturb the normal rhythm. The extra beats invariably take the form shown in Fig. 2. The tracing allows of little doubt that we are dealing with auricular extrasystoles. There is one feature, however, which should not escape attention; it will be seen that at the points at which *a* and *r* waves fall together, the resultant waves are not identical, and this is the more noteworthy in that the first extrasystole is, if anything, earlier in its cycle than the second. This has been a common and somewhat puzzling phenomenon, and it will be further alluded to.

(G.) *The interpretation of the curves obtained shortly after the cessation of an attack.*

Numerous curves have been obtained within a few minutes of the cessation of an attack, and they all present common features. They are

* The estimation of contractile force from the height of pulse waves is not without risk. Moreover, the work done by the ventricle is modified by the rate of filling, and depends to a considerable extent upon the nature and time relation of the corresponding auricular systole.

characterised by a very notable irregularity in the sinus rhythm, apart from all question of premature beats. This is very definitely illustrated in the last part of Fig. 3, and also in the electrocardiogram (Fig. 5c). Often, portions of the curves show the irregularity of the slow time proper (Fig. 2), and a premature beat is followed by a pause (as in the early beats of Fig. 3).



Figs. 5a, b, c, and d. $\times \frac{2}{3}$ linear. Case 1. Four electrocardiograms. The right arm and left leg were used as leads. The time marking in $\frac{1}{5}$ sec. has been excised from all the curves except 5a, as the plate travelled at precisely the same rate in each. Figures 5b, c, and d show simultaneous radial curves. The curves read from right to left. Oblique dotted lines are drawn between corresponding beats in the lowest three figures.

5a was taken immediately before, and 5b directly after the cessation of a paroxysm. The rate in 5a is 200. 5c and 5d were obtained within $\frac{1}{4}$ hour of 5b. The wave P corresponds to auricular, and the waves R, S, and T to ventricular contraction.*

* The galvanometer curves were taken with an Einthoven's instrument in the Physiological Department, University of London.

Nevertheless, it is not uncommonly impossible to arrive at a definite conclusion, or to interpret, finally and satisfactorily, certain instances of mixed irregularity, such as that illustrated by Fig. 3. The electrocardiograms, which may now receive further attention, do not appreciably decrease the difficulties. The beats of the curves given (Figs. 5*b* and *d*) fall mainly into two classes. There are those which conform to the normal type (and consist of P, R, and T waves), and there are those which do not. The latter present a diminution in the height of peak R, and a corresponding increase in the depth of the notch S. The T waves show little or no variation from the normal. Again, the P (or auricular wave) is absent. When numbers of such curves are examined, it is found that these atypical individual electrocardiograms correspond, as a rule, to abortive arterial waves (as illustrated in Fig. 5*b*), but that on occasion such an electrocardiographic curve is accompanied by a notable radial pulsation (the last shown in Fig. 5*d*). It is found also that the more forcible the radial pulse beat, the more prominent is the wave R. And now attention may be especially drawn to the fact that the atypical beats show considerable variation. Briefly, in the curves possessed by the writer, there is almost every intermediate condition between the normal ventricular curve of the slow time, and the curve in which R is absent and S is fully developed; the common feature is the absence of the auricular wave P. The difficulty of the interpretation of the venous tracings may now be more manifest. Taking the evidence as a whole we may be certain that one of the main features is an irregularity of sinus rhythm. It is when we attempt to co-relate the atypical electrocardiograms with the irregularities, which, as we have already seen, present the picture of auricular extrasystoles in the venous curves, that the difficulties commence. And these are due, in part at least, to our insufficient knowledge of the appearance of the electric curve of an auricular extrasystole. Such a curve will probably depend largely upon the level at which the auricular stimulus has its origin. For instance, if the contraction originates in the auricle in the neighbourhood of the auriculo-ventricular ring and travels back towards the sinus as well as forwards towards the ventricle, an inverted auricular wave may be anticipated. Moreover, such a contraction would necessarily tend to a relatively early ventricular systole, and auricular and ventricular contraction would be in some measure coincident. That this explanation is the most rational which we can hold in explanation of the present curves is suggested by the presence of a well-marked dip, in certain of the atypical beats, which directly precedes R. It is seen in some degree in all the atypical beats figured. The view tentatively put forward is that this represents the beginning of auricular contraction, and that the contraction is reversed in direction in the auricle. A downwardly directed wave is thus superimposed upon the normal *ventricular* electrocardiogram, which results in a reduction of the peak R, and a corresponding increase of the peak S. If the dip is in reality due to the commencement of auricular contraction, then the P-R interval is unduly curtailed. In the venous curve, so far as can

be seen, the *a-c* interval is of normal length. The reason for the full interval in the neck is possibly due to early appearance of the "a" wave as a result of retrograde auricular contraction, but more probably to a prolongation of the presphygmic interval, such as is well known to occur as an accompaniment of extrasystole of the ventricle in animal experiment.* We may finally conclude that the atypical beats are extrasystoles, and that they probably have their origin in the auricle, in the neighbourhood of or slightly above the auriculo-ventricular node, and that the position of origin is in all probability variable within certain limits. The question cannot be carried beyond this stage with profit in the present state of our knowledge, and the final interpretation must ultimately depend upon new observations.

Before leaving the question of the electrocardiographic curves attention must be directed to one consideration. The beats of the paroxysm are accompanied by P waves, and are at once identified as of an entirely different nature to the atypical beats discussed. The difference is enhanced by the prominence of R and the absence of T in the former curves. The last-mentioned peculiarities of the paroxysmal beats also raises the question of the nature of the distinction between these curves and those of the slow time which are normal in outline.

(H.) *The interpretation of transition tracings.*

Tracings of the transition from the paroxysmal to the slow pulse rate, and from slow to fast rate have been obtained, and are exemplified in curves 6, 7a and b, and 8.

Before proceeding to a closer examination of the curves, certain explanatory remarks are necessary. The curves are small and somewhat more obscure than those already discussed. And this necessarily follows. For to secure such tracings entails the taking of thousands of feet of curve. Thus, the tracings which have been given as illustrative of the slow pulse rate and paroxysm itself are pieces chosen for their clearness from a large collection, while a transition tracing when caught may be good or bad according to chance. The knowledge acquired, as a result of frequent and prolonged observation of the variations which may be shown in amplitude of excursion, etc., is of considerable importance in an individual case in arriving at a certain analysis of occasional curves, such as those which we may now proceed to consider.

The first part of Fig. 6 is merely a reduced example of paroxysmal

* The variation in presphygmic delay accompanying extrasystolic contractions and the subsequent large beat, in man, is usually very definite and very considerable. The statement is based upon a detailed examination of a large number of cardiographic and arterial curves, and applies to ventricular as well as to auricular extrasystoles. It is sufficient to account for many of the variations in *a-c* interval, which have been noted by Mackenzie¹, and ascribed to another cause. The variation is obviously a factor of importance in the interpretation of venous tracings, and has received less attention in the past than it deserves.

curve, and is identical with that shown in Figs. 1 and 1a. Now when the paroxysm is present, venous curves are obtainable from a large area of the neck, and when the change comes it may be that the spot chosen for taking the venous tracing is not the best which offers for a corresponding curve during the slow time. Venous curves during the slow time are difficult to obtain, for the veins are insufficiently filled with blood. The appearance of a pure carotid tracing in the latter half of Fig. 6 is, therefore, not difficult to understand. In Fig. 8 the *a* waves at the commencement of the



Fig. 8. The termination of a paroxysm. Case I. It differs from Fig. 6, in that a *c* wave is the last in the venous tracing. The *a* waves of the slow pulse are also shown.

slow time are visible, as they also were in several other tracings. Curve 6 consequently consists of two parts. In the first third the heart's action is the same as in Fig 1. In the last two-thirds its action is similar to that shown in Figs. 2 and 3. The change from fast to slow rate is absolutely abrupt, the two parts of the figure are united by a pause of $\frac{2}{5}$ secs. During the paroxysm the venous curve terminates in an *a* wave, and it is open to doubt whether this is in reality followed by an abortive ventricular beat. In Fig. 8 the paroxysm ends with a *c* wave, and the pause is longer (namely $\frac{5}{11}$ secs.). The pause may be regarded as the time taken for the building up of the stimulus which causes the first beat of the new or slow rhythm. The variation in the length of the pauses is expressed in the following table, which is an analysis of the four changes from fast to slow time which have been caught. The figures given are taken from the radial curves and are given in $\frac{1}{5}$ sec.

| 10 last fast beats. | Pause. | Succeeding slow beats. | | | | |
|---------------------|--------|------------------------|-----|-----|-----|-----|
| 17.6 | 6.0 | 3.5 | 3.2 | 6.3 | 3.6 | |
| 18.0 | 5.1 | 3.7 | 3.4 | 3.6 | 3.5 | 3.5 |
| 17.1 | 4.6 | 3.6 | 3.2 | 3.3 | 3.4 | 3.5 |
| 15.5 | 3.6 | 3.2 | 3.3 | 3.3 | 3.3 | 7.0 |

The bearing of the variability of pause upon the nature of the change will be entered into more fully in the discussion.

The only remaining point to which attention need now be drawn is the absence of absolute relationship between the lengths of the last beats of the paroxysms and the first beats of the change. Exact halving is not present,* but *what actually occurs is a sudden transition from a fast rate to a slow rate, which bears no constant relation to it, and the two rhythms are separated by a variable pause.*

A similar interpretation is to be offered in respect of Figs. 7a and b. The two figures are separate halves of a continuous tracing. When the paroxysm starts the veins of the neck are comparatively empty, and it so happens that the venous curve is indistinct and develops gradually. Thus, in the early stages of the paroxysm the *c* waves are alone present. Later, the *a* waves make their appearance at certain phases of respiration. Finally, they become as prominent and frequent as in the early part of Fig. 6. Moreover, the radial curve is affected in this instance by the presence of marked alternation, which leads to the disappearance of alternate beats in the radial pulse. Alternation at the commencement of a paroxysm has been a common feature in the tracings taken from this patient, but in one instance commencement without alternation has been noted in the tracings. The presence of alternation in the curve now considered is fully established by a detailed examination of the two figures (7a and b). The apparently halved rate in the radial pulse gradually passes into the full rate at the very end of the curve. The *c* waves corresponding to the missed beats are visible in many parts of the tracings, as are also the *a* waves which precede them. The continuation of curve 7b is identical with the first part of Fig. 6. It is consequently perfectly clear that the rate as indicated by the radial pulse at the beginning of the paroxysm is but half the sinus rate, and that the latter is approximately constant over the space shown in the figure.

In brief, the onset of the paroxysm is in every respect similar to its offset, and consists solely in the breaking through of the new or paroxysmal rhythm. As applies to the other transition there is no absolute numerical relationship between the fast and slow rhythm.

(1.) *The alterations of pulse rate directly before and after the onset or offset of paroxysms.*

A consideration of this subject is of importance in attempting to solve the actual cause of the paroxysm itself.

20-2-09. *Pulse rates every 10 secs., as measured from continuous curves :—*

194, 193, 198, 197, 198, 194, 196, 193, 194, 190, 202, 89, slow rate continued for 5 minutes, the actual change to fast rate again was not recorded ; fast rate for 15 minutes ; 194, 197, 200, 200, 191, 191, 193, 90, slow rate continued for 15 minutes ; 81, 181, 198, 207, 207, 204, 201, 201, 204, 202, etc.

* Hoffmann's view is considered in the sequel.

13-3-09. *Pulse rates every 20 secs., as measured from continuous curves :* -

Patient supine. 181 ; sitting, 200, 196, 191 ; lying, 193, 171, 171, 90 ; slow for 40 secs., 82, 181, 206, 187, 176, 182, 180, 183, 192, 180, 170, 175, 170, 181, 170, 167, 84 ; slow rate for 60 secs. : 80, 187, 200, 188, 181, 176, 176, 180, 177, 176, 179, 170, 167, 181, 175, 174, 183, 171 : sitting, 170, 182, 191 ; lying, 187, 181, 172, 176, 183, 176, 91, continued slow for remainder of observations.

These figures demonstrate the relative constancy of fast and slow rates, and show *the absence of any definite acceleration or retardation of rate as a precursor of a transition from one rate to the other.*

(J.) *The relationship of the pulse rate to systolic blood-pressure.*

The observations from this point of view have been numerous.

The average of thirty-two observations of systolic blood-pressure, taken during paroxysms with the Martin's modification of the Riva-Rocci instrument, is 102 mm. Hg. The average of eighty-one observations while the pulse was slow, is 111 mm. Hg., or 9 mm. Hg. higher. A number of the observations have been charted in the figures (Figs. 9-12). Fig. 10 shows hourly observations taken for a week during the hours of day nursing. With the exception of the third observation of the 26th February, the chart shows very fair constancy, and it is probable that this single high reading, 158 mm. Hg., standing as it does alone, was accidental. It raises the average for the paroxysm by a little less than 2 mm. Hg. It is to be noted that in so far as these hourly observations are concerned, the attacks are not foreshadowed by a rise or fall of pressure : further, it is shown that though as a rule the blood-pressure tends to fall slightly during the attacks, yet it may rise after the attack has started, and even continue to rise during the continuation of the crisis.

Closer observations, including periods of transition, have been obtained on one occasion only, and are represented in Fig. 12. The estimations were made every five minutes, and are consequently a truer representation of the events. There is a rise of blood-pressure of approximately 15 mm. Hg., which takes place synchronously with a 15-minute lapse of paroxysmal to slow rate. This chart is in fair agreement with the total averages already given.

We are justified in concluding that on the whole there is a slight fall of blood-pressure which is simultaneous with the onset of a paroxysm. The amount of the change is inappreciable, and is in no way sufficient to account for the attack itself, and this the more as a maintenance of such a fall is an inconstant feature, as has already been demonstrated (Fig. 10). To what then is it to be attributed. It must be remembered that the systolic pressure, alone, gives no true value, but only an approximation of mean pressure. And if the tracings of the transitions are again referred to it will be clear that the difference in the blood-pressure readings in the fast and slow rhythm

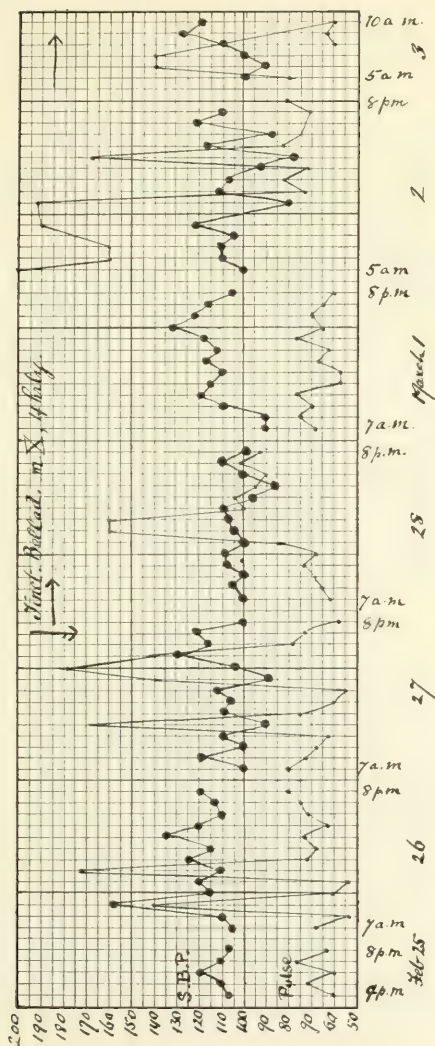


Fig. 10. Hourly observations of pulse rate and systolic blood-pressure (S.B.P.), during one week of day-nursing. The ordinates are separated by spaces each representing *one* hour. At 7 p.m. of the 27th February *incl. belladon. m X* was administered, and during succeeding days in 4 hourly doses (*i.e.*, 4 or 5 doses daily). Before the drug was given, the pulse was slow on 24, and fast on 6 occasions, a proportion according with that of Fig. 9. After the belladonna the pulse was slow on 37, and fast on 7 occasions. (The 5 a.m. and 6 a.m. observations, four of which are included in the chart, are excluded from the count.) (Case I.)

is sufficiently accounted for by the greater excursion of the pressures during the latter.

(κ.) *The influence of belladonna and aconite upon the frequency of the attacks.*

Atropine is a drug which has been administered on many occasions to patients the subject of paroxysmal attacks of tachycardia. Herringham states¹⁰ that it has even been recommended in the treatment of attacks. It was given between the paroxysms by Gerhard⁸ and by Hirschfelder without effect¹¹.

As in the last-mentioned instances, atropine was given to this patient to test the possible influence of the vagus in the production of the paroxysm. The drug was first administered (in the form of 4 hourly doses of *tinct. belladon. mX*) on the evening of the 27th February, and was continued until the evening of the 4th March, when the dose was increased to *mXV*. Now, if the sudden withdrawal of the normal tonic vagal influence is to be regarded as the sole factor responsible for the production of paroxysms, it might be expected that the exhibition of belladonna would lead to a notable augmentation of attacks. It might, indeed, be anticipated that continued paroxysm would result. The charts demonstrate that such effects are not obtainable. In the second chart (Fig. 10) the proportion of counts of fast and slow rate before and after the administration of the drug are practically identical, and in the third chart (Fig. 11) a sudden and notable decrease of the frequency of attacks is shown while full doses were being given.

The relative frequency of attacks, as shown in the chart for the 5th and 6th March, is known to have been accidental, in so far at least as the belladonna was concerned, in view of this sudden cessation and the continued abeyance over the 7th and 8th March. Further, the frequency of attacks on the 5th and 6th March (Fig. 11) was not greater than on the 18th and 20th February (Fig. 9), but, if anything, less over corresponding hours (for it must be remembered that the attacks are far more frequent during the day than the night, and the observations upon the pulse rate under belladonna were confined to the daytime). We are forced to the conclusion that the variations in frequency during the days charted were due to influences other than those of the drug administered, and it may be asserted that the view that the attacks may be due (as they have been held to be due in certain instances by Bouveret², Nothnagel¹⁶, and others) to a withdrawal of vagal influence receives no support. The evidence, such as it is, definitely points in a direction contrary to such a conclusion. Observations of a similar nature, in which aconite has been employed in doses of the tincture up to as much as *mXV* of the tincture, administered 4 hourly, have also given negative results; it has been found impossible to show that aconite has any influence in checking the attacks.

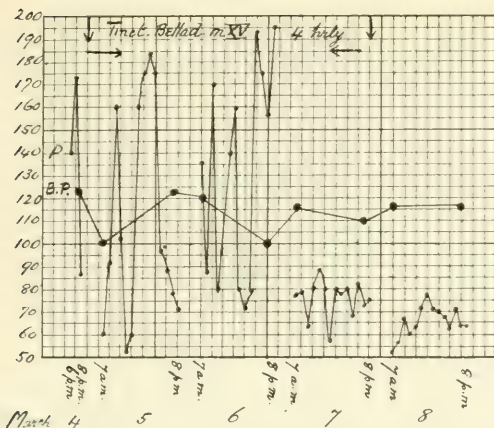


Fig. 11. Hourly observations of pulse rate (P), and occasional blood-pressure estimations (B.P.). Tincture of belladonna in doses *mX* were continued from the last day (3rd February) shown in Fig. 10, until the evening of the 4th March, when the dose was increased by *mV*. The chart shows a high percentage of paroxysm on the 5th and 6th March. That this was independent of the atropine effect is demonstrated by its cessation while the drug was continued. The belladonna was stopped on the evening of the 7th March. The counts while the drug was being given are, slow time 29, and paroxysm 15. (Day nursing only) Case I.

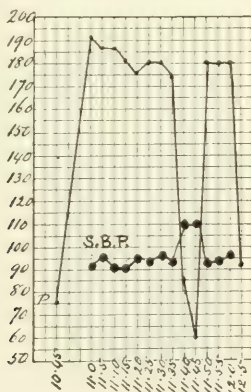


Fig. 12. Pulse rate (P), and systolic blood-pressure (S.B.P.); observations obtained at intervals of 5 minutes over a temporary suspension of paroxysm. The following notes were also made at the time. 11 a.m., marked alternation of pulse, H.A.B. internal to nipple line; 11.5, slight alternation; 11.15, H.A.B. just internal to nipple; 11.20, no alternation; 11.30, H.A.B. nipple line; 11.40, H.A.B. well internal to nipple; 11.50, marked alternation; 11.55, slight alternation; 12.0, H.A.B., internal to nipple line. Case I.

(L.) *The effect of pressure on the region of the vagus during attacks.*

Pressure on the neck in the region of both right and left vagus has been repeatedly tried during the paroxysms.* Whether of short or of long duration it has never yielded any result. In this connection it is of interest to note that two instances have been reported in which a positive result is said to have been obtained (Priesendorff¹ and Bensen¹). In opposition to the last evidence is the fact that it is usually acknowledged by writers on the subject that digitalis is without effect. Moreover, even admitting that the rapid heart action is subject to powerful vagal stimuli, this in itself is no criterion for the acknowledgment of the origin of the attacks in the withdrawal of normal impulses.

II. A CASE OF PAROXYSMAL TACHYCARDIA OF THE AURICULAR TYPE.—CASE II.

Case 2. The following brief note of a second case is published with the kind permission of Dr. Young, whose out-patient clinic the patient was attending :—

The patient, a yard-man, aged 31, states that he has not suffered from rheumatism, gout, syphilis, influenza, or the usual exanthemata of childhood. He has never been affected with dyspepsia, and has had no fits. His father is said to have died of heart disease at the age of 40. His mother, three brothers, and four sisters, are alive and healthy. He is married, and has had one child, which succumbed to diarrhoea and vomiting. The members of the mother's family have been long lived; those of the father's have died at ages from 40 to 50.

The patient himself was quite healthy until seven years ago. He used frequently to stand in the hot sun during his working hours, and experienced giddiness and faintness as a result. Subsequently he was thrown out of work during the summer months for a few days each year as a result of attacks. They usually came on with a feeling of numbness in the left arm, and at times there was general weakness and a feeling as if something was crawling over the limbs. Each attack is said to leave the limbs painful, and this sensation is more marked in the left arm, and is occasionally present over the left side of the chest. The attacks are always brought on by work, especially in hot weather. If he is able to rest he is free from them. Sometimes they are brought on by very slight exertion, and more especially when he is tired; lifting the arms over the head may be sufficient. They are accompanied by a fluttering in the cardiac region.

Physical signs.—The patient was seen by the writer on two occasions. On the first no abnormal physical signs were found in the chest, or, indeed, in any part of the system. The pulse was 80, and regular for long intervals. An occasional auricular extrasystole was noted. On getting the patient to breathe deeply, and then requesting him to hold the breath, the pulse invariably became more irregular; and on two occasions paroxysms of the auricular type occurred. They were brief in duration, and were followed by pulse irregularity of a very similar type to that found in Case I. Thus,

* The only remedy which has met with success consisted of an ice bag applied to the precordium. Cessation of the attack as a result has not been invariable.

there was sinus irregularity, and auricular extrasystoles were present. Upon the second examination the pulse was slow and regular, but on sending the patient for a sharp walk a paroxysm occurred, the pulse rate ranging from 140-150. The paroxysm continued so long as the patient was under observation. His pulse rate is said to have been at times as high as 200.

Reference is made to this case in order to illustrate two points. First, the nature of the transition from fast to slow and slow to paroxysmal rates; for the transitions are not so sharp as in the first case. And secondly, to demonstrate the presence of heart-block during the long paroxysm of which tracings were obtained on the second visit.

Description of the tracings.

Fig. 13 shows the onset of a short paroxysm, but the venous curve at the start is obscure. Following upon beats of irregular length, namely, $\frac{2.5}{5}$, $\frac{2.6}{3}$, and $\frac{2.4}{5}$ secs., are 8 beats of equal length, and occurring at a rate of 150 per minute. They are succeeded by a pause, and this is followed by a stronger beat, and two weaker ones which resemble those of the paroxysm. The same process is again repeated, and the remainder of the curve obtained was slow. All the beats are accompanied by *a*, *c*, and *v* waves, and there is a curious mixture of the stronger and slower beats, and the weaker and faster beats towards the termination of the tracing. The jugular curve gives the impression that we are dealing with three short paroxysms, and that the intervals between them are occupied by beats belonging to another rhythm. The onset and offset of the longer paroxysm, seen on the first visit, and lasting some 40 seconds, were of a similar nature.

Fig. 14 is a portion of the tracing taken at the second visit. It shows the dropping out of a single ventricular beat. It is merely an example of an occurrence which was frequent in the tracing, and which at times led for short distances to a halving of the ventricular rate. The time

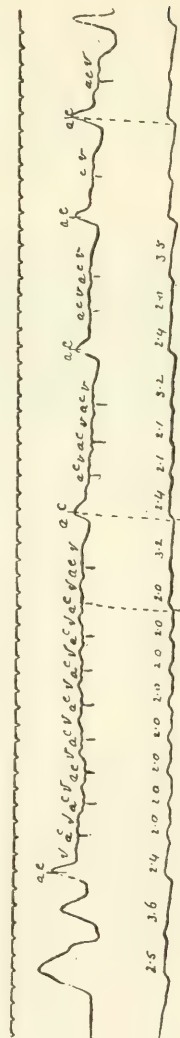


Fig. 13. Case II. The onset of a short paroxysm, showing a more gradual offset.

relations of the radial beats, and the lengths of the *a-c* intervals, demonstrate that the ventricular silence is dependent upon a defect of

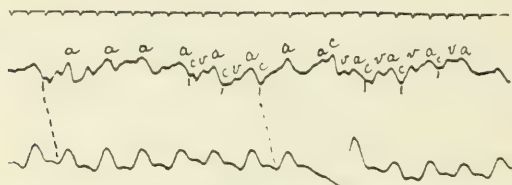


Fig. 14. Case II. Tracing taken during a paroxysm. The radial curve shows a single dropped beat. The venous curve demonstrates that the irregularity was the result of auriculo-ventricular heart-block. Pulse rate 144.

conduction, and the instance is in contrast to the dropping out of paroxysmal beats, as a result of altered contractility, already noticed.

For comparison with the first case reported the following pulse counts, as calculated from tracings, and taken shortly after the onset of the paroxysm, and continued for 38 minutes (at intervals of 1 minute), may be of interest :—

149, 150, 147, 150, 145, 147, 147, 148, 144, 148, 144, 143, 144, 140, 146, 144, 144, 143, 145, 142, 146, 145, 143, 144, 143, 145, 141, 140, 147, 145, 148, 140, 142, 142, 140, 140, 143, 145, and 140.

III. THE EXPERIMENTAL PRODUCTION OF PAROXYSMAL TACHYCARDIA.

The writer has been able to produce tachycardia experimentally in a cat and in a number of dogs by ligation of the coronary arteries, more especially the right. Such attacks, following as a rule some hour or hour-and-a-half after ligation, are preceded by extrasystoles, which may be, in the case of the right coronary, of ventricular or auricular origin. In several instances extrasystoles of auricular and ventricular origin occurred mixed with others, in which both auricle and ventricle contracted prematurely. The tachycardia, when it comes, is quite abrupt in onset, and varies in rate in different instances and under different conditions, from 140 to 400 per minute. Often it ends in fibrillation of the ventricle*, but on many occasions

* Its onset appears to be, as a rule, ventricular, and generally strong vagal stimulation fails to inhibit the ventricle, but brings the auricle to a standstill.

the normal rhythm has reappeared and reappeared abruptly. During the tachycardia, auricle and ventricle contract together; the ventricle being somewhat earlier than the auricle (as a rule by about 0.15 sec.). It would seem probable that its nature is closely related if not identical with the variety of paroxysmal tachycardia, or tachycardia, known as the ventricular or nodal form*, but so far as the observations bearing on these questions are concerned the writer prefers to reserve publication until the subject has received fuller attention.

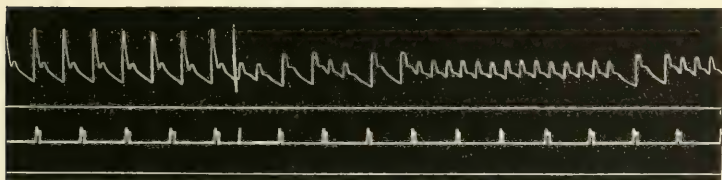


Fig. 15. Showing paroxysmal tachycardia in a cat (fully anaesthetised with urethane and A.C.E.) as a result of ligation of the right coronary artery. The curve was taken from the carotid artery by means of a Hürthle manometer. To the left of the stop the pulse rate is 90; to the right of the stop it shows a period at the rate 180. Both vagosympathetics were completely divided. The stop was of but a few seconds duration.

It is only necessary at the present time to illustrate the experiments by the curve shown in Fig. 15. The figure is a Hürthle manometer curve from the carotid of a cat, taken subsequent to the ligation of the right coronary artery, directly before and directly after the onset of the tachycardia. The points to which attention is directed, are as follows:—

1. The curve was taken subsequent to complete section of both vagosympathetic nerves. We have, therefore, an example of tachycardia produced as the result of a change intrinsic in the heart, a tachycardia which can in no way be attributed to central influences.

2. An examination of the curve before and after the onset of the paroxysm will show that the fast rate is almost if not precisely double the slow rate (the rates are 90 and 180 respectively); yet we know that the slow rate of pulse beat is the result of the normal rhythm with the normal sequence of contraction of the cardiac chambers.

These facts will be utilised in the subsequent discussion.

* The nodal form has been attributed by Mackenzie to simultaneous contraction of auricle and ventricle.

IV. THE PATHOLOGY OF THE AURICULAR FORM OF PAROXYSMAL TACHYCARDIA.

The full discussion of the pathology of the auricular form of paroxysmal tachycardia must necessarily await a detailed description of further cases, and especially those eventual findings of autopsical examination, which at the present time are completely wanting.

From the nature of the cases described, and from the observations of previous writers, it is obvious that we are in the presence of a disturbance of the heart's function, which is independent of gross macroscopic change. We have to deal with a problem in which facts, relating to the regulation of the normal heart rhythm, and to the inception of abnormal stimulus production, must be of paramount importance. It has been customary in the past to offer, in explanation of all marked variations from the normal heart rate, hypotheses consistent with our knowledge of the powerful nervous mechanism controlling the heart rate. But, with the expansion of our knowledge, the drift of recently recorded thought has tended more and more towards the emphasis of the importance of local factors. Vagal and sympathetic innervation may be potent regulators of heart rate, but can no longer be regarded as the sole determinants of its variation. Though our knowledge in this direction is still very deficient, other influences have to be acknowledged.

In the present instance it will suffice if certain of the more prominent suggested hypotheses receive examination, dealing in particular with those upon which the present observations bear.

In the first place, a few remarks may be offered as a contribution to the discussion of nervous innervation. If paroxysms of tachycardia, such as have occurred in the patient who forms the main basis of the observations recorded in this paper, are to be attributed to a withdrawal of vagal impulses*, or to an accession of sympathetic influence, then it must be conceded that such changes in nervous action may be long continued. Further, it will have to be admitted that such alterations of nervous activity must, to account for the phenomena, be almost instantaneous in their occurrence and uniform in their influence. From our acquaintance with the physiology of these nerves it would seem, at all events so far as the sympathetic is concerned, as if such admissions are barely justified. Moreover, it is open to question if, in man, suspension or the reassertion of vagal influence is sufficient to produce the wide variation of pulse rate met with in these cases†. It cannot be

* As held by Nothnagel¹⁶, Bouveret², and others.

† Bouveret², after a careful consideration of instances of central vagal affection in man, concluded that the increase of pulse rate attributable to this source, is not greater than the rate 150 to 160 (p. 844). At the same time a careful perusal of his paper, and also that of Proebsting¹⁹ will convince the reader of the intricacy and difficulty of the problem in the absence of direct evidence.

forgotten that lesions of the vagi and its nuclei have been suspected in association with paroxysmal tachycardia (the word suspected is used, as the writer, after a careful examination of such instances, is not convinced that there is a single clean case on record*), but at the same time it must be remembered that changes in the heart wall itself have been observed much more frequently. The absence of an effect from atropine, and the impotency of aconite in checking the attacks, are strong arguments against the determination of paroxysms by the withdrawal of vagal influence. The reaction of a case to aconite, which may be found in the future, and control of an attack by pressure on the vagus, such as has been already recorded by Bensen, could prove nothing more than that strong vagal stimulation may check an attack. Again, paroxysms of rapid heart action may be produced experimentally when that organ is cut off entirely from central control (as demonstrated in section III of this paper), and such rapid heart action appears to be, as a rule, beyond the control of strong vagal stimulation.

In brief, we are brought face to face with the fact that paroxysms of tachycardia or simple tachycardia may be brought about by causes intrinsic in the heart, and we have not, as yet, final proof that paroxysms can be produced in any other way. The possibility that human paroxysmal tachycardia has an origin similar to or identical with that noticed in experiment must be admitted, and, as a consequence, it becomes convenient to regard the condition as the result of a local state of irritability. And such a view receives support from several sources. A similar hypothesis has been propounded, and there is much to support it, in explanation of the companion affection, the ventricular or nodal form of tachycardia, as it occurs in man. It is also supported by the fact that single or successive extrasystoles are attributed to similar causes, and that these, like tachycardia itself, may result from the experimental production of an area of anæmic heart wall. This argument brings us at once to an important consideration, namely, the relationship of the beats of the paroxysm to so-called extrasystoles in general.

Whether the beats of the paroxysm can be regarded as extrasystoles depends entirely upon the definition of extrasystole which is adopted. If extrasystole is regarded as a term applied to any beat of the heart or part of the heart, arising as a result of stimulus production in some portion of the musculature, other than the sinus, or to abnormal stimulus production at the sinus, then there is no reason why a rapid heart action should not be looked upon as the result of a succession of extrasystoles, so long as we are satisfied that such heart beats are not of normal sinus origin. An observation

* Reference may be made to the long series of tachycardias collected by Proebsting, to Reinhold's case²⁰, in which medullary lesion and arterial disease were combined, and to other cases cited by Schmoll²¹. On the other hand, for description of the lesions of the heart, reference may be made to Herringham's collected cases¹⁰, and to Mackenzie's two cases¹¹.

which has been repeatedly made, and one upon which much stress has been laid, is the fact that when in a case of paroxysmal tachycardia the heart is beating slowly, there is a notable tendency for the appearance of extrasystoles. Let us assume that in a given case the paroxysm is due to a rapid stimulus production in an abnormal and irritable focus. It is but rational to imagine that during the slow rate an occasional beat may be thrown in from the same source. This has very probably occurred in instances of ventricular paroxysm, such as that figured by Mackenzie¹⁴ (Fig. 230), and may also account for some of the irregularity noticed in Fig. 13 of this paper. But the occurrence of an occasional extra beat during the slow pulse rate is not unequivocal evidence, though it has been used as the sole evidence, for the similar nature of the paroxysm itself. This position is fully substantiated by an examination of the electrocardiographic curves of case I. These curves demonstrate completely the wide difference between the beats of the paroxysm and those disturbing the slow rhythm. The two varieties of extra beat may be emphatically declared as of a completely different nature.

In concluding the foregoing considerations it may be said that there is evidence for regarding certain instances of paroxysmal tachycardia as resulting from intrinsic changes in the heart itself. But before we can adopt, as at the most a provisional hypothesis, the presence of an irritable focus, at one or other heart level, in explanation of certain groups of cases, there remains to be discussed a further intrinsic possibility which has been adopted more recently by Hoffmann¹².

Following the work of the eighties and nineties, upon which the strict separation of the cardiac functions is based, it has become the custom to interpret all abnormal cardiac action, so far as possible, in terms of these functions. Whether such a classification will eventually justify itself remains for the future to decide, but there can be little doubt that in many directions hypotheses based upon the independence of these functions have been suggested prematurely or upon totally insufficient data. Hoffmann first drew attention to the fact that in paroxysmal tachycardia there is a tendency for the fast rate to be double or quadruple the slow rate. But Hoffmann went further, and stated that such doubling is exact. In a series of cases the pulse rates, given in his text, show such an exact relationship. Basing his arguments upon these observations and statements he concludes that paroxysmal tachycardia is the result of a periodic failure of response of a cardiac chamber at a low level to the impulse received from one at a higher level; for example, the failure of auricular response to sinus contraction. In brief, the slow rate is attributed to an alternate failure of response, and the paroxysm itself is regarded as an expression of the usual or constant sinus rate. It will be apparent that such interference with sequential contraction may occur as the result of a theoretic deficiency of several functions, and accordingly such explanations have been offered. The proposition is at once weakened, when it is known that Hoffmann's numbers are round figures,

and that exact measurement, of some at least of the tracings given, fails to carry conviction of exact doubling or halving. Other recorded cases show an even greater divergence, and in the cases described in the present paper exact doubling or halving is far from being present. Moreover, the possibility of sino-auricular block is placed entirely out of court by the varying length of pause separating fast and slow rhythms. In the presence of true halving of sino-auricular origin the pause should bear a constant relationship to preceding and succeeding beats. Further, it will be perfectly apparent that the view cannot apply to such an example of paroxysm as that produced in the cat as a result of coronary ligature (Fig. 15). *Yet in this instance doubling of the original rate is almost, if not quite, exact* within the error of measurement. An explanation of this fact the writer is not at present prepared to offer, but he is content to record the undoubted fact.

It is, however, possible that halving and exact halving of the paroxysmal rate *may* take place, and this for reasons similar to those suggested by Hoffmann, and it is quite possible that certain of the cases of halving noted by him were of this nature. The pulsus alternans is known to occur frequently during paroxysms, and, as a result of marked alternation, alternate beats may fail to leave an impression upon the recording instrument (a fact which has also been observed in paroxysms produced experimentally in dogs). An example of this nature is given in the commencement of the paroxysm shown in Fig 7a, and the same phenomenon has also been seen during a paroxysm. But the production of a comparatively slow ventricular rhythm by this means must be carefully distinguished from the recurrence of the original slow rhythm, which is obviously of a totally distinct and specific nature. We can go yet further and state that auriculo-ventricular heart-block, due in all probability to a deficiency of conduction, may be found during a paroxysm, and may be sufficiently marked as to simulate a return to the slow or normal rhythm, in the radial pulse.

The possible production of a slow ventricular rhythm from a fast sinus rhythm by periodic failure of responses of the low level chamber has to be recognised. But it has never been shown to be anything more than temporary in duration, and, any attempt to explain the complete cardiac derangement in true paroxysmal tachycardia by the supposition of a constant increased sinus rhythm, with occasional periods during which the auricle or ventricle fails to keep the pace, can only lead observers astray from the essential feature of such cases, namely, that *we have to deal with the sudden and paroxysmal onset of an entirely new and specific heart rhythm.*

The nature of the paroxysmal rhythm, and the point at which it takes its origin, cannot be determined at present with exactitude. There is reason to believe that it differs essentially from the normal rhythm, for it is often separated from it by a lengthened pause. Moreover, a comparison of the ventricular electrocardiogram during the slow and fast rate can only lead to

the conclusion that they are distinct. The wave R is disproportionately large, and the wave T is absent during the paroxysm.

The focus from which the new rhythm arises is known to be as high as the auricle, and in view of the normal character of the wave P, is probably as high as the sino-auricular junction. Whether it lies in the collection of primitive tissue found at this site, or whether it is to be sought in the sinus itself, is a question which at present it is impossible to decide.

In conclusion, an attempt may be made to construct a collective table, which shall include those examples of new or abnormal cardiac impulses of which we have sufficient knowledge. It must be clearly understood that such a table is of the most tentative nature, and serves chiefly in giving an idea of the possible relationships of the origins of the resultant contractions one to another. Certain tachycardias are included in the list, and the inferences to be drawn from such grouping should be understood to be at present purely hypothetical. Nevertheless, as a possible interpretation of the facts, the table may be found to be not without value, laying, as it does, emphasis upon certain features displayed, either alone as characteristic of an individual type, or in common by two or more types of a single group.

The classification is based upon the assumption that all parts of the normal heart musculature are capable of giving rise to spontaneous contractions under special circumstances, and beats of this nature are included in the first category under the heading "Physiological beats." This division is further sub-divided according to whether such beats occur singly or in succession. The second division, termed "Pathological beats" (meaning by the term, beats arising as a direct result of a local morbid process) is further subdivided, according to whether such contractions are single or successive, according to whether they interfere with the normal sinus rhythm, and according to the situation in which they may be supposed to arise.

A. "PHYSIOLOGICAL BEATS."

1. *Single*. Extra beats of ventricular origin, probably arising in the lower part of the bundle, and found in cases of partial heart-block*.
2. *Multiple*. The continuous ventricular rhythm, at about 30 per minute, met with in complete heart-block (idioventricular rhythm).

B. "PATHOLOGICAL BEATS" (probably arising as a result of an irritable lesion).

- | | | | | |
|---|---|--|---|---|
| 1. <i>Single</i> (so-called <i>extrasystoles</i>). | } | a. Without interruption of sinus rhythm. | { | 1. auricular. 2. nodal or atrioventricular. 3. ventricular. |
| | | b. With interruption of sinus rhythm. | { | 1. sinoidal. 2. auricular. 3. nodal (? retrograde). |

* Contractions of this nature were described by Lewis and MacNalty (*Journ. of Physiol.*, 1908, XXXVII, 445).

| | | | | | | | |
|-----------------------------------|---|--|---|-----------------------------------|---|--|--|
| 2. Multiple and successive. | { | a. Without interruption of sinus rhythm. | { | occurrence of short duration | { | ventricular*. | |
| | | b. With interruption of sinus rhythm. | | | | 1. auricular. | |
| | { | | { | occurrence of longer duration. | | 2. nodal. | |
| | | | | | | 3. ventricular*. | |
| | | | | | { | 1. auricular form of paroxysmal tachycardia. | |
| | | | | | { | 2. nodal rhythm or <i>pulsus irre-</i> <i>gularis per-</i> <i>petuus</i> †. | |
| | | | | | { | 3. nodal or ven- tricular form of par. tachycardia. | |

CHIEF CONCLUSIONS.

1. Two forms of paroxysmal tachycardia are met with; in one the sequence of contraction of the cardiac chambers is normal; in the other the auricle fails to contract at the usual instant in the cycle.

2. In the first, or auricular form of the affection, extrasystoles occur, but their nature is different from the beats of the paroxysm. The rhythm of the paroxysm is one *sui generis*.

3. The evidence is, on the whole, opposed to the view that the paroxysm is to be regarded as the result of altered central innervation. It is more rationally ascribed to an intrinsic change in the heart itself.

4. It is probable that the rhythm between the paroxysms is the normal rhythm of the heart, and that the rhythm of the paroxysm is present during the paroxysm alone.

5. Paroxysmal tachycardia (of a ventricular form) can be readily produced experimentally by ligation of the right coronary artery, and in this condition the dog's ventricle may beat at 400 per minute. The ventricle contracts first and is followed by the auricular systole. Vagal stimulation, when the heart is in this condition, as a rule, slows or stops the auricle, while the ventricular rhythm continues unaltered.

* Such as those described in *Lancet*, 1909, i, 382.

† It is probable that this form of irregularity will subsequently require further subdivision. An electrocardiogram recently obtained from an instance of the sort shows an interruption of the usual picture by an atypical beat corresponding to the type described by Kraus and Nicolai as an extrasystole arising in the left ventricle.

BIBLIOGRAPHY.

- ¹ BENSEN. Berl. klin. Wochenschr., 1880, xvii, 248.
- ² BOUVERET. Revue d. méd., 1889, ix, 753.
- ³ COTTON. B.M.J., 1867, i, 629.
- ⁴ COWAN, McDONALD and BINNING. Quart. Journ. Med., 1909, ii, 146.
- ⁵ CUSHNY and GROSH. Journ. Amer. Med. Assoc., 1907, xlix, Fig. 15.
- ⁶ FAISANS. Bull. et mém. d. l. soc. méd. d. hop., 1890, vii, 964.
- ⁷ FALCONER. Practitioner, 1909, lxxxii, 269.
- ⁸ GERHARDT. Deutsch. Archiv f. klin. Med., 1905, lxxxii, 519.
- ⁹ HAY. Edin. Med. Journ., 1907, i, 42.
- ¹⁰ HERRINGHAM. Edin. Med. Journ., 1897, i, 366.
- ¹¹ HIRSCHFELDER. John Hopkins Hosp. Bul., 1906, xvii, 337.
- ¹² HOFFMANN. Deutsch. Archiv f. klin. Med., 1903, lxxviii, 39.
- ¹³ HOFFMANN. Zeitschr. f. klin. Med., 1904, liii, 206.
- ¹⁴ MACKENZIE. "Diseases of the Heart." London, 1908.
- ¹⁵ MACKENZIE. Quart. Journ. Med., 1908, i, 146.
- ¹⁶ NOTHNAGEL. Abstract in Sem. méd., 1887, vii, 191.
- ¹⁷ OETTINGER. Sem. méd., 1894, xiv, 421.
- ¹⁸ PREISENDORFF. Deutsch. Archiv f. klin. Med., 1880, xxvii, 387.
- ¹⁹ PROEBSTING. Deutsch. Archiv f. klin. Med., 1882, xxxi, 349.
- ²⁰ REINHOLD. Zeitschr. f. klin. Med., 1906, lix, 168.
- ²¹ SCHMOLL. Amer. Journ. Med. Sci., 1907, cxxxiv, 662.
- ²² WILLIAMS. Bristol Med. Chir. Journ., 1897, xv, 122.

THE MEASUREMENT OF SYSTOLIC BLOOD PRESSURE IN MAN.

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A CONSIDERABLE amount of discussion has taken place during the last year, as to the value of the obliteration of the pulse as an index of systolic blood pressure, the obliteration being brought about by aid of the armlet which was independently invented by Riva Rocci³, and Hill and Barnard⁴, and has since been used almost universally for the measurement of blood pressure in man. It has been asserted, and particularly by Russell⁵, Oliver⁷, Herringham^{1 & 2}, and Williamson⁹, that the rigidity of the arterial wall may be a cause of error, in that the pressure of the air in the rubber cuff may go in part to overcome the rigidity or elasticity of the wall. Russell asserts that in cases of supposed high pressure the arteries are in a state of contraction—hypertonus—and that in this state much pressure is required to squeeze together the arterial walls. Herringham and Womack² have measured the pressure required to obliterate a number of arteries obtained post mortem, and have found that while many require but a few millimetres of mercury, some require nearly 20 mm. Hg., and two even more than 30 mm. Hg. Since MacWilliam and Mackie⁶ have shown that excised arteries easily pass into a stiff condition of post mortem contraction, very much weight cannot be placed upon these figures, but Herringham¹ has recently announced that arteries, which he had soaked in a 1 per cent. solution of sodium fluoride to abolish contractility, still required pressure to obliterate them, and that this was particularly the case in degenerated arteries taken from a high pressure case. We would point out here that the index used in these experiments, namely, cessation of flow, is not the same as the blockage of the pulse wave, the index used in living man. Experiments on the blockage of the pulse wave in post mortem arteries seem to us to be required for comparison rather than experiment on the actual cessation of all flow through the artery. A pulsatile and a steady continuous flow are different phenomena. The pulse wave is transmitted by the wall of the artery, and may be, and probably is, damped down to the vanishing point before the flow is stopped.

We have sought to prove the accuracy of the systolic index in man by two methods. In one we measured the difference between the pressures in two arteries placed at different levels in relation to the heart, the proof being that the pressure differs by the hydrostatic pressure of the column of

blood which separates the two points of measurement. For it is unlikely that this would be the case if the arterial wall affects the reading, as the state of the wall varies in different arteries in pathological cases. The pressure in the two arteries is measured by us synchronously, either by palpating the radial on the dependent arm of the subject with the fingers of one hand, and the radial of the arm which is elevated with the other hand, or by utilising the radial of one arm, and the posterior tibial or dorsalis pedis of one leg—the armlets being placed on the upper arms, or one on the arm and the other round the calf. Our other method is to measure with a second armlet the pressure in the superficial veins of the forearm, while the brachial armlet is kept at a pressure 10 mm. Hg. lower than the obliteration pressure, to show that the pressure rises in these veins to the pressure in the brachial armlet, and thus to prove that the obliteration pressure is correct, at any rate within 10 mm. Hg. (Hill and Flack⁵). We have recently carried out this method on a case of slight hemiplegia with an arterial pressure of 220 mm. Hg., and have found that on keeping the brachial armlet at 200, the pressure in the veins rose to 200. We were not able to carry the venous pressure nearer than this to the arterial, owing to the painful feeling of tension caused by the rise of pressure in the limb. It is of interest to note that œdema *followed* the application of the armlet in both the foot and the hand of the paralysed side. This is the only occasion on which we have been unfortunate enough to produce œdema.

W. (male, old), suffering from cerebral hæmorrhage. The arteries feel hard.

| Obliteration pressure 220 mm. Hg. | |
|---|---|
| Pressure maintained in the brachial armlet. | Pressure obtained in the superficial veins. |
| 200 falling to | first reading 95 |
| 185 | second reading 125 |
| | third reading 165 |
| | fourth reading 170 |
| | fifth reading 180 |
| 200 | first reading 180 |
| | second reading 200 |

In all the cases to which we have applied this method, we have found no evidence of inaccuracy in the systolic index.

Williamson⁹ has recorded the pressure in the arm and leg of a fairly large number of cases, in which the pressure was high and the arteries degenerated, and has found an inequality between the two limbs, the subject being placed horizontally. The inequality was sometimes to the extent of 50 mm. Hg. Williamson did not record the pressure in the leg and arm synchronously, and, in our opinion, this is necessary, because of the varying strength of the systoles, the varying effect on the blood pressure of placing the armlet on the leg or arm respectively, etc.

Dr. Williamson has been kind enough to let us examine some of his cases. Taking the pressures synchronously, and using the radial and

posterior tibial pulses (or that of arteria dorsalis pedis) as indices, we found that, on the very first time of raising the pressure in the armlet, it took a higher pressure to obliterate the posterior tibial than the radial vessel. On allowing the pressure to oscillate up and down, and so reading the disappearance or reappearance of the pulse several times in succession (the method we always adopt), we found that the pressures became equal or very nearly equal; the reappearance of the pulse giving pressures more exactly equal than the disappearance.

*R. E. (male, old), with hard arteries and systoles of unequal force.**

(D—disappearance; R—reappearance of pulse.)

| OBSERVER | ARM. | LEG. | | OBSERVER | ARM. | LEG. |
|----------|-------|------|-----------|----------|-------|------|
| L.H. .. | D 175 | 210 | } first | M.F. .. | D 170 | 195 |
| | R 160 | 190 | | | R 155 | 155 |
| | D 160 | 160 | } reading | O.K.W. | D 185 | 195 |
| | R 135 | 135 | | | R 163 | 165 |
| | D 170 | 190 | | | D 190 | 190 |
| | R 160 | 165 | | | R 172 | 190 |
| | D 165 | 185 | | | D 187 | 187 |
| | R 150 | 155 | | | R 155 | 155 |
| | D 170 | 180 | | | D 182 | 182 |
| | R 160 | 160 | | P.C.W. | R 152 | 152 |
| | D 160 | 160 | | | D 155 | 165 |
| | D 170 | 185 | | | R 142 | 160 |
| | R 155 | 155 | | | D 172 | 175 |
| | D 155 | 170 | | | R 145 | 140 |
| | R 155 | 155 | | | | |

C. F. (male, old).

| OBSERVER | ARM. | LEG. | | OBSERVER | ARM. | LEG. |
|----------|-------|------|---------------------|----------|-------|------|
| L.H. .. | D 170 | 185 | } first reading. | M.F. .. | D 170 | 170 |
| | R 146 | 160 | | | R 155 | 155 |
| | D 163 | 180 | | | D 170 | 170 |
| | R 155 | 160 | | | R 160 | 160 |
| | D 174 | 178 | | | D 168 | 168 |
| | R 156 | 158 | | | R 158 | 158 |
| | D 175 | 175 | | | D 163 | 165 |
| | R 155 | 155 | | L.H. .. | R 160 | 160 |
| | D 168 | 174 | | | D 165 | 175 |
| | R 151 | 155 | | | R 160 | 160 |
| | D 175 | 180 | | | D 163 | 170 |
| M.F. .. | R 151 | 155 | | | R 160 | 160 |

J. S. (male, old).

| OBSERVER | ARM. | LEG. | |
|----------|-------|------|--------------------|
| L.H. .. | D 170 | 190 | } first reading |
| | R 165 | 165 | |
| | D 170 | 176 | |
| | R 165 | 168 | |
| | D 178 | 178 | |
| | R 164 | 165 | |
| M.F. .. | D 160 | 172 | |
| | R 158 | 158 | |
| | D 170 | 170 | |
| | R 165 | 165 | |

Mrs. F. (old).

| OBSERVER | ARM. | LEG. | |
|----------|-------|------|--------------------|
| M.F. .. | D 220 | 238 | } first reading |
| | R 192 | 225 | |
| O.K.W. | R 195 | 195 | |
| | D 210 | 210 | |
| | R 202 | 192 | |
| | D 210 | 225 | |
| | R 180 | 210 | |
| | D 210 | 210 | |
| | R 200 | 200 | |
| | D 195 | 208 | |
| | R 180 | 180 | |

* All observations included in this paper were made in horizontal posture, except where definitely stated to the contrary.

Mrs. B. (old).

| OBSERVER. | ARM. | LEG. |
|-----------|-------|------|
| O.K.W. | D 220 | 240 |
| | R 215 | 235 |
| | D 220 | 240 |
| | R 208 | 210 |
| | D 208 | 210 |

| OBSERVER. | ARM. | LEG. |
|-----------|-------|------|
| O.K.W. | R 195 | 195 |
| M.F. | D 210 | 205 |
| | R 195 | 195 |
| | D 205 | 205 |
| | R 195 | 198 |

We had found no discrepancy worth noting (considering the unavoidable roughness of the index) in the cases of high pressure we had examined previously, and the difference between Williamson's results and ours obviously lay in the method. He had taken first readings. We had always oscillated the pressure up and down, and taken a number of readings, and while doing so selected the reappearance of the pulse as the index.

The figures show that the obliteration pressures become somewhat lower and approximate to equality when the oscillation method is employed. The first readings show distinct differences. The results suggest that keeping the pressure on relaxes the arteries, and at first sight this seems to support the theory that the arterial wall of a contracted artery does come into play by its resistance to compression. It seemed to us, however, that the difference might be due to the better conductance of the systolic wave by an artery which is somewhat harder, than by a softer one. Also the figures seemed to show that the synchronous obliteration of the two large arteries raised the aortic pressure at first, and that then the heart might be quieted by vagus action, and the pressure lowered somewhat.

Up to this point we had never found any difference between leg and arm readings of young men placed in the horizontal position. The arteries of the legs thicken with age, and have stiffer walls than those of the arms owing to the high hydrostatic pressure of the blood in the standing posture, and thus we should expect the difference in reading to appear with advancing age if it were due to better conductance.

Holtzmann, acting on the suggestion of one of us (L.H.), made some independent observations of a similar kind and like result, in the London Hospital. He also tried the pressure in two or three cases of aortic regurgitation, and told us that he had found a noticeable difference between arm and leg reading in such.

Following up this interesting observation we have found that in all cases of aortic regurgitation there is this marked difference, which is not abolished by the method of oscillating the pressure up and down near the obliteration pressure. So marked is this difference that we believe we could pick out the cases of aortic regurgitation by it alone.

I. H. S. (male, age 33), aortic case.

| ARM. | LEG. |
|-------|------|
| D 130 | 195 |

II. W. H. (male, age 21), aortic and mitral disease.

| ARM. | LEG. |
|-------|------|
| D 120 | 136 |
| R 118 | 128 |

III. T. N. (male, age 51), aortic and mitral disease.

| ARM. | LEG. |
|-------|------|
| D 150 | 200 |
| R 154 | 204 |

IV. T. (male, young), aortic case

| ARM. | LEG. |
|-------|------|
| D 160 | 240 |
| D 150 | 220 |
| R 140 | 160 |

Right arm and left arm gave equal pressures of 140 mm. Hg.

V. F. (male, age 27), aortic case, fully compensated and about at work.

| ARM. | LEG. | |
|------|------|--------------------------------|
| 110 | 130 | when fresh and well. |
| 110 | 150 | on another day. Both legs 150. |
| 110 | 170 | when tired. |
| 106 | 156 | another day. |

Maximal pulsation over a much wider area in leg than in arm, but average of it about the same, e.g. 75—85. On setting pressure in armet at 100, pressure in veins of arm rose to 100.

VI. Young man, aortic case.

| ARM. | LEG. |
|------|------|
| 118 | 172 |

VII. W. McS. (male, young), aortic case, allowed up in ward.

| ARM. | LEG. | |
|------|----------------------|------------------------------|
| 130 | 220 (dorsalis pedis) | first reading on lying down. |
| 122 | 208 " | later. |
| 118 | 172 (poster. tibial) | when confined to bed. |
| 122 | 168 " | " " |
| 116 | 210 (dorsalis pedis) | " " |
| 116 | 190 " | " " |

VIII. A. C. (male, age 22), aortic case.

| ARM. | LEG. | |
|------|------|---|
| 136 | 178 | abduction of arm or leg (made no difference). |
| 130 | 180 | |

In the case of the leg measurements, in some cases great variations occur in the relative size of the dorsalis pedis and the posterior tibial arteries. The larger of the two must be chosen for the measurement of the index; a small posterior tibial gives a considerably lower reading than a large dorsalis pedis. We tried putting the limbs in varying postures to test whether the systolic wave passed into the leg arteries more easily with the vessels straight, but this made no difference in our results. As these inequalities occurred in young men with soft arteries, and were not abolished or lessened by keeping the pressure on, they seemed to us to be due to the better conductance of the great systolic wave by the leg arteries, which were maintained in a somewhat contracted state in order to secure an adequate blood supply to the brain.

To test this hypothesis we conceived and carried out the following experiments.

I. We made normal young men take the violent exercise of running up and down stairs several times and immediately after took the readings in the horizontal posture. As an example we may give the following instance :—

S., before and after exercise.

| ARM. | LEG. | |
|------|------|-----------------------------|
| 128 | 128 | before exercise. |
| 168 | 240 | immediately after exercise. |
| 158 | 220 | later. |
| 158 | 212 | " |
| 148 | 210 | " |
| 142 | 204 | " |
| 158 | 132? | " |
| 130 | — | " |
| 122 | 118 | " |
| 108 | 110 | " |

In another student there was no difference while resting, and one of 20 mm. Hg. after exercise.

The pressures in both his arms were equal before and after exercise, i.e., 128 mm. Hg. before, and 178 mm. Hg. after. The results showed us that the big slapping systolic wave after exercise produced in normal young men a temporary difference like that met with in aortic cases.

In a very emotional student, with a loud hæmic murmur, and nervous of our examination, we found a difference before any exercise was taken.

| ARM. | LEG. |
|------|------|
| 138 | 152 |

II. We tested the effect of softening the arteries locally by immersing the limb in hot water.

A. W., young man.

| RIGHT ARM. | LEFT ARM. | DIFFERENCE. | CONDITION. |
|------------|-----------|-------------|--|
| 128 | 128 | 0 | quiet. |
| 178 | 178 | 0 | after stair climbing. |
| 120 | 124 | 4 | right hand and wrist in hot water, left in iced water. |
| 170 | 198 | 28 | after stair climbing. |

The difference disappeared as the heart quieted down.

Only the hand and wrist were put in the hot water, and the flushing was limited to these parts. It might, however, be objected to the conclusiveness of this experiment that the brachial artery was also relaxed reflexly by putting the hand in hot water. We disproved this by repeating the hot water experiment, and taking the systolic index in both the radial and the brachial at the elbow of one arm. The systolic index disappears in the radial softened by heat before it does in the brachial, and this is particularly the case when the systolic crest is augmented by exercise.

If the elbow be heated locally the systolic index is still equal in both radial and brachial, but is at a lower level than before, as the conductance is damped down in the softened brachial. This is a most convincing proof that it is the conductance of the pulse wave, and not the resistance of the artery to compression that is at the bottom of the phenomena we have been considering.

A. W., young man.

| | | BRACHIAL. | RADIAL. | |
|-----------|----|-----------|---------|--|
| Left Arm | .. | 110 | 110 | quiet. |
| | | 160 | 160 | after stair climbing. |
| | | 140 | 136 | after hand in hot water |
| | | | | 118° F., radial feels much softer. |
| | | 150 | 130 | hand in hot water and after climbing stairs |
| | | 152 | 130 | hand bandaged firmly. |
| Right Arm | .. | 126 | 114 | hand cooling. |
| | | 112 | 112 | quiet. |
| | | 158 | 158 | after stair climbing. |
| | | 134 | 134 | after elbow in hot water and stair climbing. |

W. M., young man ; athlete ; standing.

| | | BRACHIAL. | RADIAL. | |
|-------------|----|-----------|---------|---|
| Right Arm | .. | 138 | 138 | quiet. |
| | | 138 | 126 | after hand and wrist in hot water 118° F. |
| Left Arm .. | .. | 137 | 137 | quiet. |
| | | 126 | 126 | after elbow in hot water 118° F. |
| | | 124 | 124 | " " |
| | | 126 | 126 | " " |

A. W., young man.

| | LEFT ARM. | RIGHT LEG. | |
|--|-----------|------------|---|
| | 124 | 124 | quiet. |
| | 120 | 120 | |
| | 110 | 120 | after hand and wrist in hot water. |
| | 110 | 130 | " " |
| | 104 | 124 | " " |
| | 110 | 120 | " " |
| | LEFT ARM. | RIGHT ARM. | |
| | 150 | 190 | after left hand in hot water, and stair climbing. |
| | 150 | 170 | later*. |

* The pressure in the arteries of the right arm and right leg were then almost equal.

We next sought to lessen the difference in aortic cases by a hot water foot bath, and succeeded in doing so.

F., young man: compensated aortic case.

First observation.

| ARM. | LEG. | |
|------|---------|----------------------------|
| 110 | 170 | quiet. |
| 110 | 140 | after foot in hot water. |
| 110 | 160-170 | foot cooled by cold water. |

Second observation on another day.

| ARM. | LEG. | |
|------------|-----------|-------------------------|
| 110 | 150 | quiet. |
| RIGHT LEG. | LEFT LEG. | |
| 150 | 150 | |
| 170 | 170 | reading raised after |
| | | keeping pressure on. |
| 130-150 | 80-90 | after keeping left foot |
| | | in hot water for |
| | | some minutes. |

M., young man; aortic case.

| LEG. | ARM. | |
|-------|------|----------------------------|
| 208 | 122 | quiet. |
| 208 | 122 | " |
| 152 | 120 | after foot in hot water. |
| 162 | 120 | later, foot cooling. |
| D 140 | 122 | after foot in hot water. |
| R 138 | 118 | |
| 170 | 120 | after pouring cold water |
| | | on foot, but foot flushed. |
| 162* | 120 | later. |
| 158 | 120 | " |

* The right leg gave 190.

In this patient the dorsalis pedis was the larger in the left foot, and the posterior tibial in the right foot. There was a difference of 18 mm. Hg. between the small posterior tibial and the large dorsalis pedis of the left foot.

In the case of one elderly man with chronic Bright's disease, and a very high blood pressure, we found the leg reading 20 mm. higher than the arm; and this difference was not abolished by keeping the pressure on and was only lessened a little by putting the foot in hot water. The foot flushed but little in comparison with that of a young man.

| ARM. | LEG. | |
|---------|------|--------------------------|
| 240-250 | 270 | |
| " | 264 | after foot in hot water. |

In another case (aged 69), with aortic aneurysm and pressure of 210 mm. there was no alteration after placing the hand in hot water.

CONCLUSIONS.

The conclusions we draw from these experiments are as follows :—

1. We have no evidence that the resistance of the arterial wall to compression affects the systolic index of blood pressure.

2. The relative softness or hardness of the arterial wall affects the conductance of the systolic wave markedly, and so modifies the readings. This is particularly the case when the systolic wave is a large one.

3. The arm and leg readings are the same in young men when quiet and in the horizontal posture. They differ by the hydrostatic pressure of the column of blood which separates the points of measurement in the standing or inverted posture. We have shown that in the vertical postures the leg pressure varies greatly, while the arm pressure is kept about the same by the mechanism which compensates for the influence of gravity on the pressure of the blood in the left ventricle and cerebral arteries⁵.

4. The arm and leg readings differ after the violent exercise of stair climbing and in aortic cases because the big systolic waves are conducted better down the leg arteries—these being slightly thicker or more contracted and rigid.

5. A difference between arm and leg readings is most marked in all cases of aortic regurgitation, and when such patients are lying quiet in bed this difference is a diagnostic sign of aortic regurgitation.

6. The difference can be brought out in normal young men by softening the arteries locally by placing either the hand or foot in hot water. The experiments with hot water prove that the difference is due to conductance of the systolic wave. The difference so called out is made much greater by increasing the amplitude of the systolic wave by exercise. Hot water makes little difference in the case of some old men with high pressures; their arteries do not soften.

7. The difference may be found in the case of old folk with degenerate arteries and high pressure, at the first reading, but is abolished in almost every case by keeping the pressure of the armlet on. For this relaxes the leg arteries and reflexly lessens the force of the systole, and so lessens the difference in the conductance of the wave.

8. In reading systolic pressures there are two factors to take into account, (1) the actual maximal pressure of the cardiac output; (2) the conductance of the pressure wave by the artery. The force of the wave is damped down in soft arteries, as sound waves are damped by velvet.

9. Blood pressure readings should be taken, therefore, under uniform conditions with patients lying horizontally, not emotionally excited, not after exercise, not after taking hot food, tea, coffee, or alcohol, not after the hand and wrist have been warmed or chilled. Comparatively synchronous

readings of hand and foot arteries, the effect on the readings of oscillating the pressure up and down, and the effect of local heat gives information as to the state of the arteries, the value of which will grow with extended clinical observation.

BIBLIOGRAPHY.

- ¹ HERRINGHAM. Proc. Roy. Soc. Med., 1909, II., 238 (Med. Sect.).
- ² HERRINGHAM and WOMACK. *Ibid*, 1908, II, 37 (Med. Sect.).
- ³ RIVA ROCCI. Gaz. Med. di Torino, 1896-7.
- ⁴ HILL and BARNARD. Lancet, 1898, I. 282.
- ⁵ HILL and FLACK. B.M.J., 1909, I, 272; Proc. Physiol. Soc., 27th Feb., 1909.
- ⁶ MACWILLIAM and MACKIE. B.M.J., 1908, II, 1477.
- ⁷ OLIVER. "Studies in Blood-pressure," London, 1908 (2nd edit.).
- ⁸ RUSSELL. "Arterial Hypertonus, Sclerosis and Blood-pressure," Edin. and London, 1907.
- ⁹ WILLIAMSON. Proc. Roy. Soc. Med., 1909, II, 229 (Med. Sect.).

THE REGULAR OCCURRENCE OF INTERPOLATED EXTRASYSTOLES.

By E. E. LASLETT.

(Hull.)

A VENTRICULAR extrasystole is usually followed by the so-called compensatory pause. In 1889, however, Wenckebach¹ pointed out that ventricular extrasystoles may be interpolated between normal rhythmic beats of sinus origin, and the compensatory pause is then absent. He gave the following explanation. When the heart is beating infrequently, and the refractory phases of the ventricle are relatively far apart, it is possible for the extrasystole to fall in such a way that the excitability and contractility of the heart-muscle have partially recovered when the next physiological stimulus arrives; as a consequence the contraction following the extrasystole does not fail, and the compensatory pause is absent. His conclusions were drawn from radial curves. In 1903, Trendelenburg², using the suspended frog's heart, cooled the sinus and produced slowing of the heart rate. By stimulating the ventricle he was able to produce interpolation of the resulting extrasystole. In the same year, Pan³ described further instances of interpolation in the human subject, accompanying slow sinus rhythm. His curves show numerous extrasystoles, some of which are followed by a compensatory pause, and some of which are interpolated. In 1905, Hering¹ and Rihl¹ wrote upon this subject. The former stated that instances of interpolation had been observed in man at normal pulse rates, but that usually the pulse rate is slow, and that the interpolated extra-beat occurs early in diastole. Rihl gave tracings showing the interpolation produced experimentally in the mammalian heart. Venous tracings have been published by Pan⁴, and more recently by Mackenzie². The former observed interpolated extrasystoles occurring after every single and after every second normal beat.

I have at present under my care a patient suffering from mitral stenosis, in whom this form of extrasystole has been not only of frequent occurrence, but has also appeared at regular short intervals during comparatively long periods. The patient is a married woman, aged 40, who has never been pregnant. She has had two attacks of chorea, the first at 20 years of age. At the present time her chief symptoms are palpitation, dyspnoea on the slightest exertion, some degree of cyanosis, and slight oedema of the feet. The heart is somewhat enlarged to the right. Occasionally there is a presystolic murmur, but more usually a systolic murmur with a loud first

sound at the apex. The liver is enlarged and pulsatile, and there is marked tenderness on pressure over it. The curve of the pulsation is of the auricular type (Fig. 1). The pulse is small, and, when the patient is at rest, rather slow (60 to 70). On many different occasions the pulse has shown numerous intermissions, due occasionally to auricular, but much more commonly to ventricular, extrasystoles of the usual type. At times there have been long series of interpolated extrasystoles occurring regularly after every third normal beat. I have observed this rhythm present for 2 minutes without a break. On one occasion it persisted almost continuously for several days

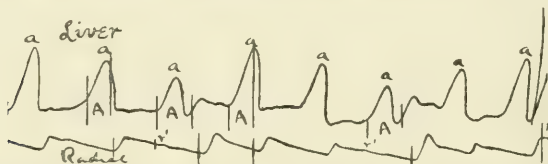


Fig. 1. Simultaneous tracing of the liver and radial pulses. Commencement of a series of interpolated extrasystoles. The A interval is much increased after the interpolation. (D., 22nd December, 1908.)

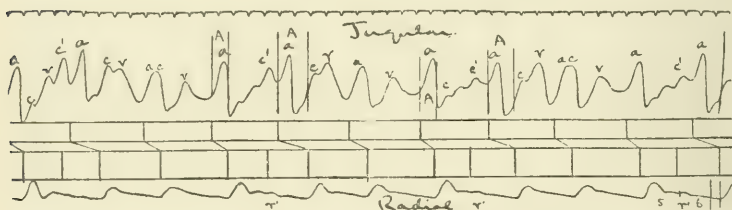


Fig. 2. Simultaneous tracing of the jugular and radial pulses. Portion of a long tracing during which an interpolation occurred after every third normal beat. The a-c interval, after the extrasystole, is about $\frac{2}{3}$ sec.. (D., 6th October, 1908.)

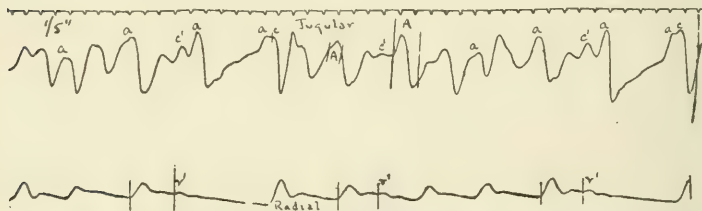


Fig. 3. Simultaneous tracings of the jugular and radial pulses. An extrasystole occurs after every third normal beat. In the two instances in which there is a compensatory pause the extrasystole occurs nearly $\frac{1}{2}$ sec. later than the interpolated beat. (D., 6th October, 1908.)

(Fig. 2). Occasionally the extrasystole is followed by a compensatory pause, and in some such instances, as Dr. Mackenzie has pointed out to me, the premature beat occurs slightly later than usual (Fig. 3).

In this patient there appears to be a great tendency towards the regular appearance of extrasystoles, whether followed by a compensatory pause or not. The most common type is an extrasystole with a pause after every second normal beat. If we take into consideration the missed ventricular beat which gives rise to the compensatory pause it is clear that the extrasystole appears after every third physiological stimulus, that is to say, with the same frequency as in the interpolated series. When the interpolations are less regular in their appearance there are, every now and then, short periods during which they appear with their usual frequency after every third normal beat. Sometimes again, the interpolations appear after every sixth beat, and in correspondence with this it is common for extrasystoles followed by a pause to appear after every fifth normal beat, that is, counting the missed beat, after every sixth physiological interval. It is thus evident that the extra-stimulus tends to appear after every third or every sixth normal stimulus interval; in some instances the following normal beat fails, in some it does not.

In his cases of interpolated extrasystoles Mackenzie² found a prolongation of the *a-c* interval following the extrasystole. In the present case it is evident from the figures that the *a-c* interval, after the interpolation, is markedly increased, being equal to two-fifths of a second. This defective conductivity does not appear to be the rule, and in this connection it may be mentioned that in tracings from a patient of advanced age under my care, in whom interpolated extrasystoles occurred after every fourth normal beat, the prolongation of the *a-c* interval following the interpolation was much less marked, and in some instances it was scarcely demonstrable. As there is a rheumatic history in the present case it is possible that there may be damage to the A-V bundle, which may, to some extent, account for the defective conductivity after the extrasystole; for the possible influence of retrograde conduction from the point of origin of the extra-stimulus, upon the A-V bundle, must be borne in mind. The prolongation of the *a-c* interval is clearly connected with the occurrence of an extrasystole which is not followed by a compensatory pause, but in the present state of knowledge the precise significance of this factor in relation to the origin of the compensatory pause is not apparent. Further facts are necessary before a completely satisfactory explanation is forthcoming.

CONCLUSIONS.

1. Interpolated extrasystoles may occur at regular intervals just as do those followed by a pause.

2. There is, in the case considered, marked prolongation of the *a-c* interval following the interpolated extrasystole. This, however, does not appear to be the rule, and the exact significance of this factor with regard to the origin of the compensatory pause is not at present clear.

BIBLIOGRAPHY.

- 1. HERING. Zeitschr. f. exper. Path. u. Therap., 1905, 1, 26.
- 2. MACKENZIE. Quart. Journ. Med., 1907-8, 1, 131.
- 3. PAN. Deutsch. Archiv f. klin. Med., 1903, LXXVII, 128.
- 4. PAN. Zeitschr. f. exper. Path. u. Therap., 1905, 1, 57.
- 5. RIHL. Zeitschr. f. exper. Path. u. Therap., 1905, 1, 43.
- 6. TRENDLENBURG. Archiv f. Anat. u. Physiol., 1903, Phys. Abth., 311.
- 7. WENCKEBACH. Zeitschr. f. klin. Med., 1899, XXXVII, 181.

THE RATE OF BLOOD FLOW IN THE ARM.

By A. W. HEWLETT AND J. G. VAN ZWALUWENBURG.

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IN 1907, T. G. Brodie¹ described a new method for determining the rate of blood flow through an organ. The latter was placed in an oncometer which was connected with a volume recorder, its efferent vein was suddenly occluded, and its changes in volume recorded. The progressive swelling of the organ represented the rate at which the arterial blood entered. At first this was comparatively rapid, but gradually it became slower and slower, owing to the rise of pressure in the veins, capillaries, and surrounding tissues. The first portion of such a record represents the normal rate of arterial inflow. Brodie believed that this method gave as reliable results as the *Stromuhr*, but that it was only applicable to organs from which all the efferent blood could be collected by a single vein.

We have attempted to apply the Brodie principle to the arm of man². The arm is placed in an ordinary plethysmograph, and changes of volume are recorded by a volume recorder. The details of the apparatus are shown in Fig. 1. After making certain that the apparatus does not leak, a pressure cuff, similar to that used in determining the arterial pressure by the Riva-Rocci method, is placed about the arm above the plethysmograph, and a pressure is applied, which is well above the venous pressure and, at the same time, well below the diastolic arterial pressure. It is assumed that such a pressure occludes the veins but leaves the arteries open, and that the resulting changes in the volume of the arm, for a time at least, represent the rate at which the arterial blood enters. Under proper conditions this rate of inflow remains approximately constant until a certain amount of blood has entered; after which the swelling proceeds less rapidly, in some instances because blood begins to escape beneath the pressure cuff, in others because the inflow is impeded by the increasing pressure in the veins, capillaries, or tissues.

In order to obtain satisfactory records by this method, certain technical details must be observed. In the first place, the curves are often marred by respiratory movements. These are mainly, if not altogether, due to the mechanical thrust or pull of the arm in the plethysmograph, caused by respirations, and are diminished or avoided by changing the position of the latter, if necessary swinging it from above. In the second place, the pressure in the cuff must be applied very suddenly in order that the veins

may be occluded from the start. This is accomplished by connecting the cuff with a large bottle in which the pressure has been previously raised above that desired for the cuff. When the stop-cock between the two is opened, the pressure is applied to the arm almost instantaneously. In the third place, the application of the pressure is often followed by an immediate change in the volume of the arm within the plethysmograph. In some instances there is a shrinkage due to a drawing of the tissues out of the

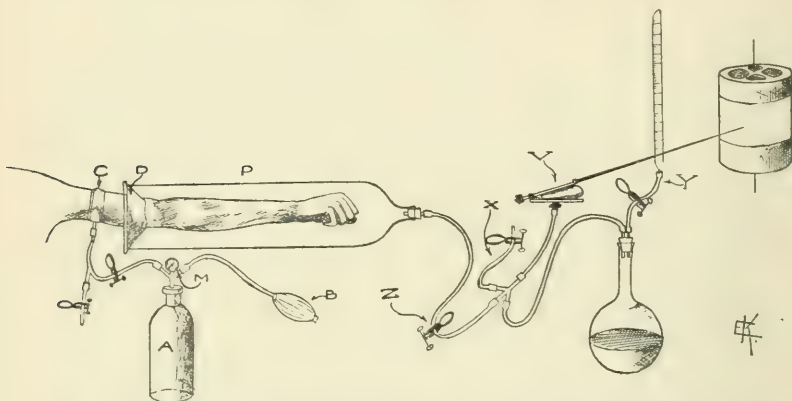


Fig. 1. Diagram of apparatus for determining the rate of blood flow through the arm. The arm is placed in the plethysmograph, P, the opening of which is closed by a piece of rubber dam, D, and the connection with the skin made tight with soap-suds. The narrow pressure cuff, C, is placed around the arm about 3 cm. above the opening into the plethysmograph. The pressure cuff is inflated by opening the stop-cock connecting it with the large bottle, A, in which the pressure has previously been raised by the rubber bulb, B. Pressures are read by the spring manometer, M. The plethysmograph is connected with the volume recorder, V, which writes upon a moving drum. Air can be let out of the system by the stop-cock, X, and water can be introduced from the burette, Y, so that the writing point of the volume recorder can be adjusted at will. The stop-cock, Z, serves to disconnect the plethysmograph from the recording apparatus during adjustments of the former. The recording apparatus is graduated by allowing 5 cc. of fluid at a time to flow in from the burette, and marking the elevation of the volume recorder thus produced.

plethysmograph by the tightening of the cuff. In other instances there is a swelling due to the crowding of the tissues or tissue fluids into the plethysmograph. This last was especially troublesome when a 12 cm. cuff was used and deformed the curves so much that we finally came to use a narrow 3 cm. cuff, placed about 3 cm. from the membrane covering the end of the plethysmograph. Under any circumstances the first portion of the curve is apt to be deformed to some extent by the sudden application of pressure, and the first few centimeters of change in the arm volume is to be

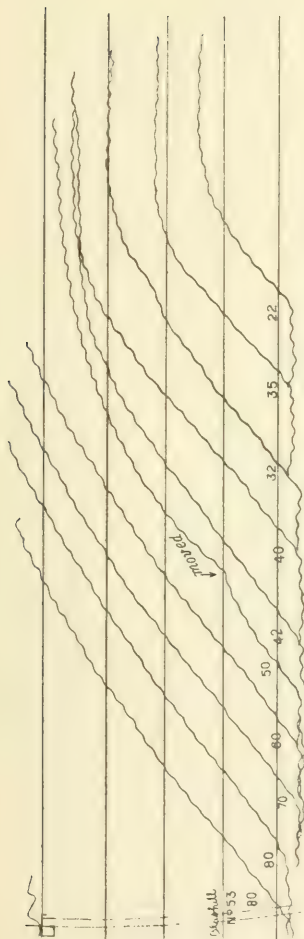


Fig. 2. $\times \frac{1}{2}$ linear. Tracings showing the effect of different cuff pressures. The first are parallel, the later ones tend to become horizontal, owing to the escape of venous blood beneath the cuff. The numerals represent the pressures applied by the pressure cuff. Each space between the straight horizontal lines represents 5 cc. increase in arm volume. The time record was inadvertently omitted.

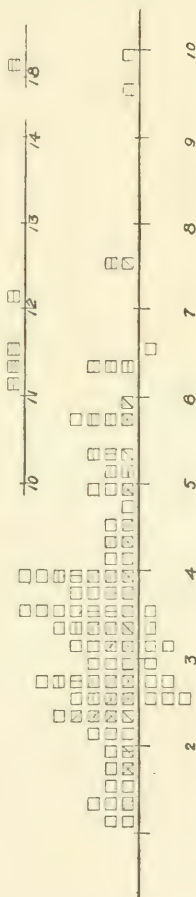


Fig. 3. Charted results of the determination of rates of blood flow through the arm. Normal individuals are placed below the line. The following symbols for different diseases are used: Nephritis \square , Heart Diseases \square , Anemia \square , Exophthalmic Goitre \square , Neurasthenia \square . Complications are indicated by combinations of more than one of these symbols.

disregarded should it fail to tally with the later swelling. Finally, it is important that the inflow of arterial blood should not be checked too soon by the rise of pressure in the veins and capillaries, else the rate of arm swelling begins to diminish almost from the start, and it is difficult to say what is the normal rate of unimpeded inflow. It was found that this retardation could be greatly delayed if the arm were slightly elevated above the horizontal. Under these circumstances the veins are partially emptied, and a reservoir is created for the accommodation of new blood. Fifteen to twenty cubic centimeters will often enter without a retardation greater than 20 per cent. of the original inflow.

The general accuracy of this method depends mainly upon the answer to the question—Are the veins occluded and the arteries left open by the pressure cuff? As has been said this is accomplished theoretically, provided the pressure in the cuff is above the highest venous pressure and below the lowest arterial pressure. A series of different pressures lying between these two points should cause the same changes in the volume of the arm: whereas, if the veins are only partly closed, or the arteries not completely left open, a variation in the pressure applied should modify the course of the swelling. As a matter of fact it was found that within certain limits the pressure applied by the cuff made no difference in the rate of arm swelling. For example, in Fig. 2 the curves obtained with pressures of 80, 70, and 60 mm. mercury are all parallel, while those with lower pressures are parallel to a certain point, when the curve begins to fall off owing to the rise of venous pressure and the consequent escape of blood beneath the pressure cuff. We believe that in all of these curves the arteries were wide open, and the veins closed for a time at least. In our observations two, and usually three or four records were taken at different pressures in the cuff, most frequently between 40 and 70 mm., and unless the curves obtained at different pressures were substantially parallel the records were rejected. The time was marked in seconds, and the record graduated each time by clamping off the plethysmograph and allowing 5 cc. of water at a time to run into the bottle from the burette. The spaces between the parallel horizontal lines, therefore, represent 5 cc. of arm swelling. The volume of the arm within the plethysmograph was then measured, and the rate of inflow for each 5 cc. was calculated in terms of the number of centimeters of blood which entered each hundred cubic centimeters of arm substance in one minute. Applying this method of calculation to Fig. 2, we obtained the following table:—

| Pressure in Cuff. | Rate of Inflow per 100 cc. arm substance per minute. | | |
|----------------------|--|--------------|-------------|
| | First 5 cc. | Second 5 cc. | Third 5 cc. |
| 80 | 9.6 cc. | 9.2 cc. | 8.7 cc. |
| 80 | 9.2 cc. | 8.7 cc. | 7.8 cc. |
| 70 | 9.7 cc. | 9.2 cc. | 8.7 cc. |
| 60 | 9.6 cc. | 8.7 cc. | 7.6 cc. |
| 42 | 9.6 cc. | 8.2 cc. | |

A glance at this table shows the substantial agreement between the figures obtained at different pressures in the cuff. It shows, furthermore, the tendency of the blood to enter at diminishing rates as the vessels become distended. Indeed, this tendency introduced so large an error with the fourth 5 cc. that these were omitted from the calculations. The cause of this gradually lessening rate at which the arm swells, when high pressures are applied, is due mainly to the accumulation of blood in the vessels. We disregarded this slowing of the inflow provided it fell within 15 to 20 per cent. of the rate at which the first 5 cc. entered.

Fig. 3 represents in graphic form the rates of flow in the arms of normal and pathological individuals. The majority of these showed a rate between 2 and 4 cm. of blood flow per 100 cc. of arm substance per minute. Those below the base line represent the flow in a group of normal young individuals. With one exception these all showed a rate of about 3 cc. per 100 cc. per minute. Our figures agree fairly closely with those of Tschewsky, who used the *Stromuhr* on the legs of dogs, and obtained inflows averaging 3.25 cc. per 100 cc. of leg substance per minute, and varying between 1.93 cc. and 4.77 cc. under normal conditions, but increasing to as much as 11.8 cc. after cutting the nerves, and 6.89 cc. after a brief obstruction of the artery.

As might be expected, the rate of inflow varies greatly in a given individual under different circumstances. In some persons, especially those who show dermatographia and flush easily, there is often a continual change in the rate of inflow. This may manifest itself on a single record or on succeeding records. In such instances the Traube-Hering vasomotor waves are usually well marked. For example, in one individual the rates of inflow on two successive records were as follows:—

| Pressure. | First 5 cc. | Second 5 cc. | Third 5 cc. | Fourth 5 cc. |
|-----------|-------------|--------------|-------------|--------------|
| 60 | 2.7 cc. | 4.0 cc. | 4.1 cc. | 4.8 cc. |
| 60 | 4.3 cc. | 4.9 cc. | 2.4 cc. | 2.1 cc. |

These variations, which amounted to 100 per cent., were evidently due to the marked vasomotor instability, as was shown by the large vasomotor waves obtained in the ordinary plethysmographic tracing taken from him.

Exercise of the forearm within the plethysmograph is followed by a very marked acceleration of the blood flow (Fig. 4). That this is a local effect for the most part, is shown by comparing it with the flow observed when the opposite forearm is correspondingly exercised.

TABLE SHOWING THE EFFECT OF EXERCISE.

| No. of Experiment | .. | (1) | (2) | (3) | (4) | (5) |
|-----------------------------|----|---------|---------|---------|---------|----------|
| Rate before exercise | .. | 1.8 cc. | 2.3 cc. | 2.4 cc. | 2.6 cc. | 3.5 cc. |
| Rate after exercise of same | | 4.5 cc. | 8.5 cc. | 7.1 cc. | 8.1 cc. | 27.3 cc. |
| and of opposite arm | | | 3.9 cc. | 2.3 cc. | 3.9 cc. | |

It will be seen from this table that whereas exercise of the arm opposite to that within the plethysmograph produced little or no acceleration of the blood flow, exercise of the arm that is within the plethysmograph caused a most decided acceleration, amounting to from three to eight times the normal rate of flow. This acceleration passes off fairly rapidly after cessation of the exercise, though the normal rate is not reached for some minutes. Successive determinations of the rate after exercise in No. 4 gave 8.1 cc., 5.8 cc., and 4.1 cc. In No. 5 they gave 27.3 cc., 19.0 cc., and 10.4 cc. Our observations on the effect of exercise upon the local rate of blood flow correspond with those obtained experimentally by Chauveau and Kaufmann², who collected the blood coming from the "releveur propre de la lèvre supérieure" of the horse, and found that during the act of voluntary chewing the flow was increased from four to nine times the flow during rest. They greatly exceed the changes during or following interrupted or continuous faradic stimulation of the cut nerves leading to the muscle³. As Tschuewsky suggests, this difference may be due to a vasodilator action accompanying voluntary innervation of the muscles.

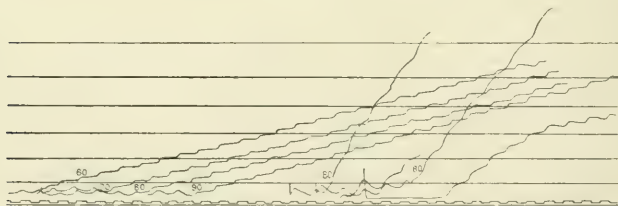


Fig. 4. $\times \frac{1}{3}$ linear. Tracings showing the effect of exercise. The first four were taken during rest, the following ones at short intervals after resistance exercises of the hand within the cylinder.

The effect of the local application of heat upon the flow of blood through the arm was tested in several instances, by thrusting the arm into very hot water, and then taking the rate of flow as soon after as the apparatus could be applied. It was found that the arm, which had presumably become swollen in the hot water, began to shrink almost immediately after being taken out, so that it was difficult to say how much conditions had changed by the time the records were taken. A moderate increase in rate was usually found. Thus, in one individual the rate before thrusting the arm in hot water was 3.7 cc. per 100 cc. of arm substance per minute, while the readings taken immediately after were, 5.9 cc., 5.7 cc. and 4.7 cc. In another individual the rate before was 3.0 cc., and after was 5.0 cc.

The application of heat to the body as a whole is a more effective and certain method of increasing the rate of flow through the arm (Fig. 5). The

most striking results were obtained in an individual who was placed in a very hot tub bath, and left there about 10 minutes, at which time he began to complain of a sense of fullness in the head. Previous to the bath his arm rate had been 3.1 cc. of blood per 100 cc. of arm substance per minute. Subsequent to the bath, with a body temperature of 103.8°, his rate was 15.6 cc. Still later, after his temperature had fallen to 101.2°, the rate was 13.6 cc. This patient showed no effects of the application of heat.

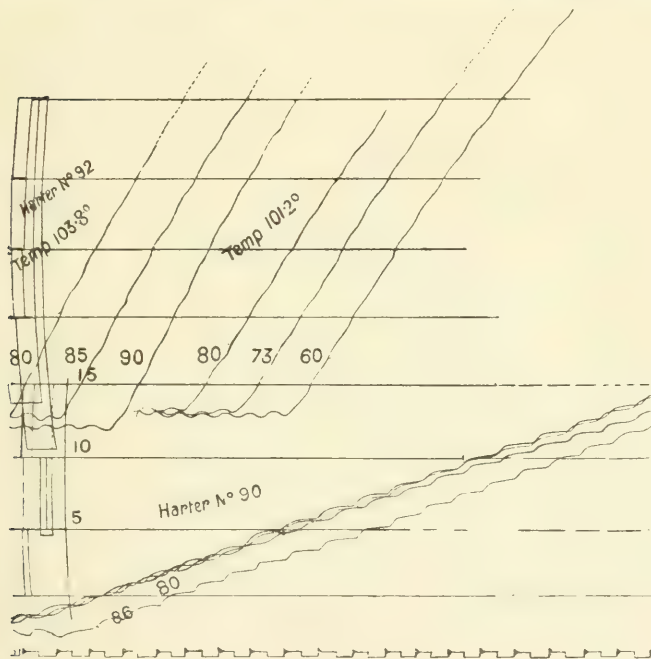


Fig. 5. γ linear. Tracings showing the effect of a hot bath. Series "No. 90" taken before the bath; series "No. 92" after the bath.


other than a feeling of fulness in the head, profuse perspiration, and a general feeling of warmth. We are inclined to believe that similar accelerations in the peripheral circulation are by no means uncommon during hydrotherapeutic procedures, where much heat is added to the body. In another individual, after moderately fast walking on a hot day, and after

a rest of about 15 minutes without cooling, the rate of flow through the arm was 6.45 cc. per 100 cc. of arm substance per minute, while after cooling it fell to 2.6 cc. Still another individual showed a rate of 6.8 cc. on a hot day, and this fell to 4.6 cc. after cooling.

The variations in the rate of blood flow through the arm of a given individual can be approached in another way, viz., by comparing the rates obtained at different times on the same individual. Our results are tabulated below :—


| TABLE SHOWING, IN VERTICAL COLUMNS, THE VARIATION IN ELEVEN INDIVIDUALS FROM TIME TO TIME. | | | | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|------|-----|-----|-----------|
| Observation No. | (1) | (2) | (3) | (4) | (5) | (6) | (7) | (8) | (9) | (10) (11) |
| 1.2 | 1.9 | 2.0 | 3.2 | 3.2 | 3.2 | 3.5 | 5.2 | 5.4 | 5.4 | 9.5 |
| 1.5 | 2.9 | 2.2 | 3.4 | 3.8 | 4.9 | 5.4 | 12.0 | 5.8 | 7.5 | 11.0 |
| 2.7 | | 3.2 | | | | | | | | 18.0 |
| 3.1 | | | | | | | | | | |

It will be seen that variations of 50 per cent. are not uncommon, while variations of 100 per cent., or even more, may occur. Some of these variations are to be explained by changes in the condition of the individual. For example, No. 11 was a patient with exophthalmic goitre, who came to the hospital with a rate of 18 cc. per 100 cc. of arm substance per minute. After rest in bed, with medical treatment, this fell to 11.0 cc., and after removal of a part of the thyroid gland it was found to be 9.5 cc. Nos. 8 and 10 were pronounced neurasthenics, with labile vasomotor systems. It is difficult to explain many of the other variations, for the patients were at rest, though it seems not unlikely to us that temperature and humidity may have exercised a considerable influence, the rate being faster on warm days. Indeed, any condition which necessitates increased elimination of heat from the body, such as a large meal, exercise, or excitement, would probably lead to variations in the peripheral blood flow. Such uncontrollable variations introduce a serious source of error when one tries to compare the rates in different individuals, or in the same individual, under varying circumstances.

Our observations on the blood flow in the arms of different individuals are tabulated in Fig. 3. They are arranged according to the rate of flow. The normal individuals are placed below the base line. The symbols within certain squares denote certain pathological conditions. Patients with chronic nephritis, designated by , interested us on account of the possibility of finding some relation between the rate of flow and the high blood pressure. Our findings in this class of patients are given in the following table :—

| TABLE SHOWING RATES IN CHRONIC NEPHRITIS. | | | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| No. of observation | (1) | (2) | (3) | (4) | (5) | (6) | (7) | (8) | (9) |
| Age | 34 | 48 | 57 | 48 | 52 | 54 | 47 | 61 | 57 |
| Systolic pressure | 120 | 138 | 164 | 176 | 180 | 200 | 220 | 234 | 245 |
| Diastolic pressure | 90 | — | 106 | 120 | — | — | 150 | 188 | 147 |
| Pulse rate | 120 | — | 68 | 66 | — | — | 90 | — | 65 |
| Rate of flow in arm | 1.9 | 3.1 | 4.0 | 2.3 | 3.2 | 3.2 | 4.9 | 4.4 | 5.8 |
| | | | | | | 3.8 | 2.7 | | 5.4 |

It will be seen that the rates for these individuals cannot be considered particularly abnormal, although in a very general way the rate of flow increased slightly with the higher blood pressures. This increased rate, however, was by no means proportional to the increase in blood pressure, and one must conclude that the blood stream met with more than the normal resistance in the arms of these patients.

In patients with heart disease the rate of blood flow in the arm was usually about normal, even though well marked valvular lesions were present, or the heart showed the absolute and permanent form of arrhythmia. Our results are shown in Fig. 3, and are designated by . In two patients the rate was taken during badly broken compensation. One showed a rate of 1.3 cc., distinctly below the normal; the other showed a rate of 2.5 cc.

In anæmia the rate of flow through the arm is of particular interest, for the reason that Kraus¹ and Plesch⁶ have recently claimed that the output from the heart is greatly increased in severe anæmias, even up to five times the normal. Our figures for the arm, though showing on the whole a somewhat rapid rate of blood flow, are far short of that described by these authors for the general circulation:—

TABLE SHOWING RATE OF BLOOD FLOW IN THE ARMS OF ANÆMICS.

| | | | | | | |
|------------------|-----|-----|-----|-----|-----|-----|
| Per cent. of Hb. | 22 | 48 | 50 | 60 | 70 | 70 |
| Rate of flow .. | 3.7 | 2.7 | 3.8 | 3.5 | 3.5 | 5.4 |

All of these patients, except the second, had pernicious anæmia.

Having discussed the rates in nephritis, heart disease, and anæmia, there remain for consideration the unusually slow and the unusually rapid rates. Those below 2.0 cc. per 100 cc. of arm substance per minute belong to the former category. Eleven of these were recorded, occurring in a number of different pathological conditions. Two were severe diabetics, two advanced gastric carcinomas, one an advanced nodular sclerosis of the radial arteries, one a patient with valvular heart disease with absolutely irregular rhythm and badly broken compensation, one a patient with partial heart-block, etc. The main factors possessed in common by these patients, so far as we could discover, were moderate emaciation, asthenia, and a cool, dry skin. With the two exceptions mentioned they presented neither signs nor symptoms of cardiac insufficiency.

The more rapid rates, over 5 cc. of blood flow per 100 cc. of arm substance per minute, were relatively more numerous, occurring in 23 of our observations on 18 different patients. The fastest rate occurred in a patient with a severe form of exophthalmic goitre. On admission his rate was 18.0 cc. per 100 cc. of arm substance per minute, after rest in bed and medical treatment his rate was 11.5 cc., and after removal of a portion of the thyroid gland it was 9.5 cc. A second patient, with a pronounced form of this disease, showed a rate of 11.3 cc., while a third, with a very mild

form, showed a rate of 5.8 cc. We suspect that this acceleration of the peripheral rate of blood flow is a fairly constant feature of exophthalmic goitre, and roughly proportional to the severity of the disease.

TABLE SHOWING THE RATE OF FLOW IN THE ARM IN EXOPHTHALMIC GOITRE.

| Patient. | Age. | Systolic Pressures. | Diastolic Pressures. | Pulse rate. | Flow. | Remarks. |
|----------|------|---------------------|----------------------|-------------|----------|---------------------------|
| (1) | 28 | | | | 5.8 cc. | Mild case. |
| (2) | 27 | | | 110 | 11.3 cc. | Severe case. |
| (3) | 37 | 176 | 96 | 140 | 18.0 cc. | Severe case. |
| | | 178 | 93 | 144 | 11.5 cc. | After medical treatment. |
| | | 190 | 112 | 128 | 9.5 cc. | After surgical treatment. |

A majority of the remaining fast rates occurred in neurasthenics of the vasomotor type, individuals who flush and perspire easily, and who usually have warm, moist skins. In order to test the hypothesis that young individuals of this type have relatively rapid rates of flow through the arm, four students of a vasoneurotic type were examined, and of these three showed rates over 5.0 cc., while the fourth showed a rate of 3.9 cc.

In undertaking this study, we had hoped that it would assist in throwing light upon the rate of blood flow in the body as a whole. A review of our results, however, seems to emphasize the predominating influence of local conditions. The slow rates were found most often in those who had cool, dry skins, while the fast rates occurred in those with warm, moist skins. It is difficult to compare the local rate of blood flow with the general rate in man, for the reason that we have no satisfactory method for estimating the output from the heart. In over half our patients the systolic and diastolic pressures were taken with the Erlanger instrument; and the difference between the two, the pulse pressure, was multiplied by the heart rate. It has been claimed that this product is roughly proportional to the total systolic output from the left ventricle. We failed, however, to discover any relation between this product and the rate of flow in the arm, as determined by our method. This discrepancy might be caused either by a true lack of relation between the peripheral blood flow and the systolic output from the heart, or else by a large error in either of the methods used. We are inclined to agree with O. Müller¹ in his view that the pulse pressure is practically useless as a means of comparison of the systolic outputs of different individuals.

CONCLUSIONS.

We believe that the method here described determines the rate of peripheral blood flow in the arm with rough accuracy, the error in favourable cases not exceeding 20 per cent. By means of this method it is possible to demonstrate in man the tremendous acceleration of the local blood stream following exercise, as well as that which occurs in overheating by the general hot tub. It has been possible to show that the rate of peripheral blood flow is not markedly influenced by the high blood pressure of nephritis, by heart disease, except in the extreme stages of broken compensation, or by anemias of the pernicious type. On the other hand, emaciated, asthenic patients, with cool, dry skins generally have a slow rate of flow through the arm; while those with exophthalmic goitre and the vasomotor type of neurasthenia generally have a rapid flow.

BIBLIOGRAPHY.

- ¹ BRODIE (T. G.). The determination of the rate of blood flow through an organ. Reported at the Seventh International Physiological Congress, August, 1907.
- ² CHAUVEAU and KAUFMANN. *Compt. rend. de l'acad. des sciences*, 1887, civ, 1126.
- ³ HEWLETT and VAN ZWALUWENBURG. Method for estimating the blood flow in the arm. *Arch. of Internat. Med.*, 1909, iii, 254.
- ⁴ KRAUS (F.). Die Methoden zur Bestimmung des Blutdrucks beim Lebenden und ihre Bedeutung für die Praxis. *Deutsch. med. Wochenschr.*, 1909, xxxv, 235.
- ⁵ MÜLLER (O.). Der arterielle Blutdruck und seine Messung beim Menschen. *Ergeb. d. in. med. u. Kinderheilk.*, 1908, ii, 367.
- ⁶ PLESCH (J.). Hemodynamische Studien. *Zeitschr. f. exper. Path. u. Therap.*, 1909, vi, 380.
- ⁷ TSCHUEWSKY (J. A.). Ueber Druck, Geschwindigkeit, und Widerstand in der Strombahn der Arteria carotis und cruralis so wie in der Schilddrüse und im Musculus gracilis des Hundes. *Archiv f. d. ges. Physiol.*, 1903, xcvii, 210.
- ⁸ TSCHUEWSKY (J. A.). Ueber die Aenderung des Blutstroms im Muskel bei tetanischer Reizung seines Nerven. *Archiv f. d. ges. Physiol.*, 1903, xcvii, 289.

THE EXPERIMENTAL PRODUCTION OF PAROXYSMAL TACHYCARDIA AND THE EFFECTS OF LIGATION OF THE CORONARY ARTERIES.*

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THE observations, upon which the following communication is based, were briefly outlined in the first number of this *Journal*.

Certain effects were noted as the result of tying one or other coronary artery in cats, during the progress of some experiments undertaken with a different object. A number of investigators had already worked at the effects of obstructing the main vascular supply to the heart walls, but as no analysis of the actual irregularities produced had been attempted up to the time when the present observations were commenced, it was considered advisable that a more detailed examination should be made.

A full account of the work already accomplished in the direction of coronary artery ligation will be found in Porter's article⁶, and in the more recent publication of Miller and Matthews⁵. A discussion of these observations will not be undertaken, for they are of a different nature to those upon which emphasis is to be laid in the following pages.

The detailed analysis of the irregularities obtained, as a result of coronary artery ligation, was considered of importance for several reasons. The irregularities which occur are in a measure spontaneous, for they are the outcome of the production of a continuous abnormal process in the heart wall, and do not result from interrupted mechanical or electric stimulation. As a consequence, a closer resemblance to the irregularities met with in clinical study might be anticipated, and the conditions giving rise to them could be considered as being more nearly allied to those which prevail in disease. The careful study of any abnormal rhythm, produced by experimental damage to the heart itself, must of necessity be useful, if it can be shown that a similar rhythm may occur in natural pathological conditions. It was also anticipated from the preliminary experiments that a lesion might be found, which would yield a permanent or paroxysmal increase of heart rate with sufficient constancy to allow a more complete investigation of such a tachycardia to be made. This expectation has been fulfilled.

* The expenses of these investigations have been defrayed by a grant from the Royal Society.

Our knowledge of clinical tachycardias of abrupt onset and offset is by no means complete, and the experimental side of the question has remained practically untouched; if such a tachycardia could be obtained with regularity, a study of it, at whatever level it might have its origin, would materially assist us in understanding the factors which operate in the production of the two main types of paroxysmal tachycardia known to occur in the human subject.

In the present communication, therefore, attention will be chiefly restricted to an abnormal and rapid action of the heart, which is a result of interference with its vascular supply.

METHOD.

During the course of these experiments dogs have been employed exclusively, both on account of the facility with which the coronary vessels are reached, and because of the ease with which reliable records can be obtained from the separate chambers of the heart in this animal. The animals were narcotised with morphia and paraldehyde, and these anæsthetics were supplemented with ether in sufficient quantity to produce complete or deep surgical anæsthesia. The carotid artery was connected to a Hürthle manometer, and, in certain instances, a special plethysmograph was employed to enclose the left external jugular vein in such a way that records of venous volume could be obtained. The sternum was split longitudinally and the sides of the chest wall were drawn apart, the pericardium was opened and stitched to the chest wall. A loose ligature was placed around the coronary artery, or branch of the coronary artery selected, after the necessary blunt dissection had been accomplished. Stitches were placed in the right auricle (one in the tip of the appendix, and one at the base of the appendix) and in the ventricles (one at the right and one at the left border of heart). By means of these stitches, the points of the special myocardiograph levers, devised by Cushny (modified from Roy and Adami's pattern), were secured to the musculature of the auricle and ventricle. The levers give the most reliable record obtainable of muscular shortening, and they work independently of general movements of the viscus examined. These preparatory arrangements occupied as a rule from $\frac{3}{4}$ to 1 hour. A preliminary tracing was taken, which included a curve from auricle and ventricle, a carotid pressure curve, and, upon occasion, a venous volume curve. Subsequently the ligature was tightened, and subsequent events were recorded. In the last experiments the carotid curve has been replaced by a galvanometer curve, and the auricular and ventricular movements have been recorded photographically by means of the original myocardial levers, working in front of the same slit. For the electrocardiograms, Edelmann's latest pattern of Einthoven's string galvanometer has been utilised. The body current was led from the right forepaw and left hind paw, by means of baths of saturated sodium chloride solution in which the terminals were immersed. The vagosympathetic nerves were invariably divided during the course of the experiment.

At the termination of an experiment the heart was placed in formalin, and the successful application of the ligature was subsequently verified.

GENERAL OUTLINE OF THE EFFECTS OF THE LIGATION.

Two arteries have been dealt with, namely, the descending branch of the left coronary, and the right coronary artery near its origin.

In the case of the descending branch of the left vessel a patch of muscle, which lies entirely in the ventricular muscle, is damaged. In the case of the right coronary the area devascularised includes the right auricle and the greater part of the right ventricle. A narrow strip of healthy muscle remains in the right ventricle directly to the right of the interventricular groove. When the ligature is tightened an immediate change in the colour of the implicated muscle is seen as a result of the obstruction to its blood supply. From a slight cyanotic tinge, the colour passes rapidly to a lividity, which is maintained during the remainder of the experiment (the accompanying veins are usually included in the ligature). Within a few minutes the damaged ventricular muscle dilates and is ballooned. With each systole of the heart it becomes more swollen, until eventually no visible contraction is present. The right auricle continues to beat, but the strength of its contraction is usually diminished. When, at the end of an experiment, fibrillation ensues, the damaged ventricular muscle fails to participate in the fibrillation.

The accompanying table gives a list of experiments, and in each instance shows the vessel tied, the time of onset of the first irregularity, the time of onset of the first paroxysm of tachycardia, and, finally, the time at which the experiment terminated or was abandoned.

Five experiments were performed in which the descending branch of the left coronary was selected for ligation. In one instance paroxysms of tachycardia were obtained (Dog C). In the sixth experiment the right coronary was occluded, but no paroxysm was produced. It was not until the seventh experiment (Dog G) that the importance of the time factor was fully recognised, and in the remaining instances sufficient time was allowed for the development of that condition which appeared to predispose to the production of the tachycardia desired. The table gives the results of observations upon seventeen animals in all. In five the left coronary, and in twelve the right coronary was ligatured. In one of the former, and in nine of the latter tachycardia was obtained.*

In the experiments in which the descending branch of the left coronary artery is tied, the resultant irregularity takes the form of ventricular extrasystoles, and with the exception of the tachycardia in one experiment, no other form of arrhythmia has been observed. The extrasystoles are at first single, occurring at varying instants in diastole. Later they are multiple and successive. Groups of two, three, and four are frequent. At times a

* In a later experiment similar results to those of Dog R were obtained.

TABLE I.

| Dog | Coronary tied | Time of occurrence of first extrasystole after ligation. | Time of onset of paroxysm after ligation. | Time and nature of cessation of experiment after ligation. |
|-----|-------------------|--|---|--|
| A. | Desc. br. of L.C. | 4 m. | — | 1 h. 10 m. Experiment stopped, heart beating normally. |
| B. | Desc. br. of L.C. | 5 m. | — | 7 m. Ventricular fibrillation. |
| C. | Desc. br. of L.C. | 44 m. | 1 h. 17 m. | 4 h. 14 m. Experiment stopped, rhythm normal. |
| D. | Desc. br. of L.C. | 2 m. | — | 48 m. Ventricular fibrillation. |
| E. | Desc. br. of L.C. | 3 m. | — | 37 m. Experiment stopped. |
| F. | R.C. | 2 m. | — | 1 h. Experiment stopped. |
| G. | R.C. | 3 m. | 1 h. 25 m. | 1 h. 56 m. Ventricular fibrillation. |
| H. | R.C. | 22 m. | 1 h. 37 m. | 2 h. 12 m. Ventricular fibrillation. |
| I. | R.C. | 32 m. | 1 h. 10 m. | 1 h. 25 m. Ventricular fibrillation. |
| J. | R.C. | 15 m. | 15 m. | 45 m. Auricle faradised, experiment stopped. |
| K. | R.C. | 3 m. | 1 h. 13 m. | 3 h. 13 m. Ventricular fibrillation. |
| M. | R.C. | 44 m. | 2 h. 6 m. | 3 h. 9 m. Experiment stopped. |
| N. | R.C. | 27 m. | — | 1 h. 46 m. Ventricular fibrillation. |
| O. | R.C. | 21 m. | 37 m. | 57 m. Ventricular fibrillation. |
| P. | R.C. | 20 m. | 32 m. | 1 h. 45 m. Ventricular fibrillation. |
| Q. | R.C. | 10 m. | — | 2 h. 30 m. Experiment stopped. |
| R. | R.C. | 20 m. | 1 h. 11 m. | 1 h. 12 m. Ventricular fibrillation. |

bigeminy or trigeminy* results. Occasionally retrogression to the auricle occurs (retrograde extrasystoles).

Obstruction of the right coronary vessels yields irregularities of greater variety. Auricular extrasystoles, ventricular extrasystoles, early or late in ventricular diastole, occur in profusion; extrasystoles in which auricle and ventricle contract prematurely and together, or in which the ventricle precedes the auricle, are common. Bigeminy and trigeminy, as a result of one or other form of extrasystole, are seen. Interpolated extrasystoles are rare. Groups of two or more auricular or ventricular extrasystoles, and other groups in which auricle and ventricle contract together, are numerous. Complex irregularities in which auricular and ventricular extrasystoles appear

* The bigeminy was produced as a result of an extrasystole following each normal beat; the trigeminy was produced as a result of an extrasystole following every two normal beats.

independently and in close proximity to each other are occasional. Publication of the curves illustrating these arrhythmias is deemed unnecessary, and a full description of the more complex instances is postponed.

At present, attention will be directed to those experiments in which tachycardial paroxysms were obtained, namely experiment C, and experiments G, H, I, J, K, M, O, P, and R. Protocols giving selected chronological detail are included in an appendix.

GENERAL DESCRIPTION OF THE PAROXYSMS.

It has been seen that the paroxysms are produced with considerable frequency when the right coronary vessels are tied. Thus, they were obtained in nine out of twelve experiments. Some time must be allowed to elapse before such paroxysms may be expected. In the majority of instances the requisite time, subsequent to the interference with the vascular supply, exceeds one hour. In three cases it was less, and amounted to 15, 37, and 32 minutes respectively. The failure to obtain tachycardia in all but one of the early experiments upon the left coronary is attributed to the too early abandonment of most of these experiments. In the ten animals in which tachycardia was obtained, it ended in ventricular fibrillation during the first attack in four instances only (cp. Table II). In the remaining six, the normal rhythm was re-established. In their recurrence the paroxysms were most frequent in the fifteenth experiment (Dog P). In this animal eight attacks were noted. In duration the paroxysms vary from a few seconds to 35 minutes. The average rate (first taking averages for each individual, and finally averaging all) was 253, the average of the normal rhythm (similarly calculated) was 126*. Frequently the ventricular rate exceeds 300, and at times the contractions follow each other at a rate passing 400 a minute. In Fig. 6 the frequency is 397, and the auricle is in fibrillation. The ventricle beat later at 405, and passed imperceptibly from this rhythm into fibrillation. Such was the termination also in the experiment from which Fig. 16 is taken. The rate as shown is seven beats per second, or 420 contractions per minute. As a general rule the rhythm of the ventricle during the paroxysm is regular, and frequently each beat is followed by a systole of the auricle, at an interval which varies slightly from experiment to experiment. As a rule the Vs-As interval (the interval between the onset of ventricular and auricular systole) lies between 0.10 and 0.16 sec.; the average for the ten experiments was 0.139 sec.. In one instance, included in the table, a longer period (0.28 sec.) was noted, but in this it was open to question as to which ventricular beat was the cause of the auricular response. On the other hand the As-Vs interval for the preceding normal rhythm lies between 0.07 and 0.12 sec.; the average was 0.098 sec.. The Vs-As interval in

* As will be seen from an examination of Table II, the almost doubled rate during the paroxysms is much more exact in the averages than in the individual instances. In the single instance previously reported the doubling happened to be exact.

any given experiment has exceeded, almost invariably, the As-Vs interval of the preceding normal rhythm by a small fraction. The Vs-As interval remains fairly constant from experiment to experiment: it also remains approximately the same while wide changes in the ventricular rate occur. The As-Vs interval during the paroxysm varies indirectly to the rate.*

THE IRREGULARITIES IMMEDIATELY PRECEDING THE ONSET OF THE PAROXYSMS.

As a rule, the irregularities which lead up to the paroxysm are extrasystoles starting in the ventricle. In the earlier stages single, in the later stages multiple and successive, they become more and more numerous. Generally, after a short run of beats (from 2 to 4) retrogression to the auricle takes place. This phenomenon is clearly depicted in Fig. 1, where the second beat of a pair originates a response on two occasions (cp. Fig. 14). Retrogression also occurs in Fig. 2, representing the onset of a paroxysm. To the left of the last mentioned figure are three extrasystolic ventricular beats, each retrograde to the auricle, followed by a pause with return to the normal rhythm. The normal rhythm is promptly interrupted again by similar beats, and in the last part of the figure they lead directly into what actually became a continuous paroxysm with alternation. The tendency for the spontaneous ventricular beats to induce auricular contractions is, to a large extent, independent of the rate of the sinus rhythm, and also of the instants at which they appear, though certainly not entirely independent of these factors. Once reversal has shown itself, it recurs with increasing frequency.

THE ONSET OF THE PAROXYSM.

The record of the abrupt onset of a paroxysm of tachycardia of short duration is obviously more difficult to obtain than is that of its offset. With the latter there is a warning of its impendence, while in the former there may be none. It is requisite that the drum should travel at a speed adequate for the mensuration of intervals, and the duration of an experiment precludes a continuous record at such a rate. Subsequent to the ligation of the artery the heart is watched, and samples of the irregularities are obtained from time to time. When it comes, the paroxysm is immediately recognised by the quick and regular rolling movement of the heart which it creates. As a consequence, the majority of the records start a second or so after the actual onset, and at times, therefore, certainty of the manner of onset may be

* In ascertaining whether A responds to V, or V to A, considerable stress is laid upon the constancy of the Vs-As interval or As-Vs interval. In fast paroxysms the two intervals may be almost equal. If A is responding to V, with constant Vs-As intervals, during a paroxysm of varying rate, then the As-Vs interval of the same paroxysm must show variation, necessarily dependent upon the variation in the rate of the paroxysm.

absent. Moreover, the onset is not invariably in the same fashion. The commencement in individual cases is almost uniform in one respect; ventricular extrasystoles lead up to it. But they may or may not be numerous, and on one or two occasions were not recorded. Fig. 2 represents the commencement of the fourth paroxysm in Dog K. It shows the transition of retrograde extrasystoles* into the beats of the actual paroxysm. The

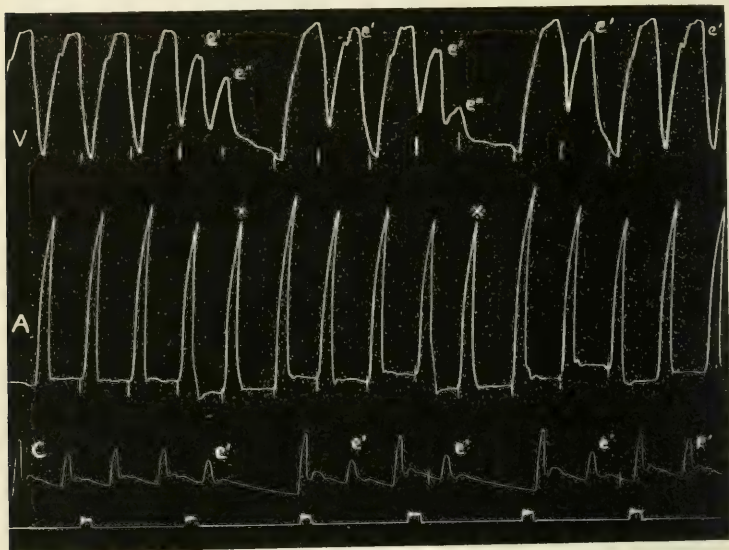


Fig. 1. Dog M; 1.15. V, curve of muscular shortening in ventricle; A, the same in the auricle. C, Hürthle curve from carotid. The movements are all upright. The time marking is in seconds. The figure shows the normal rhythm interrupted by extrasystoles, which prevailed for over an hour before the onset of the paroxysm. This example shows seven ventricular extrasystoles (e' and e''). In two instances a pair of extrasystoles is shown. The second beat of each pair (e'') is retrograde to the auricle (the premature auricular beat is marked \times) and fails to effect the carotid pressure. The As-Vs interval is less than the Vs-As interval of the two retrograde beats. In this curve, as in several others, the time tracing is uneven. This is not due to irregularity in the movement of the drum or time pendulum, but to a slight delay in the movement of the time signal at alternate beats. The inequality escaped observation until it was too late to remedy it.†

close resemblance between these preliminary contractions and the systoles of the paroxysm itself at the end of the curve (the paroxysm was continuous from this point onwards) is very striking, both in respect of

* Extrasystoles which start in the ventricle and appear to awaken an auricular response.

† The setting of the events depicted in any given figure may be examined by reference to the protocol of the experiment to which such a figure belongs.

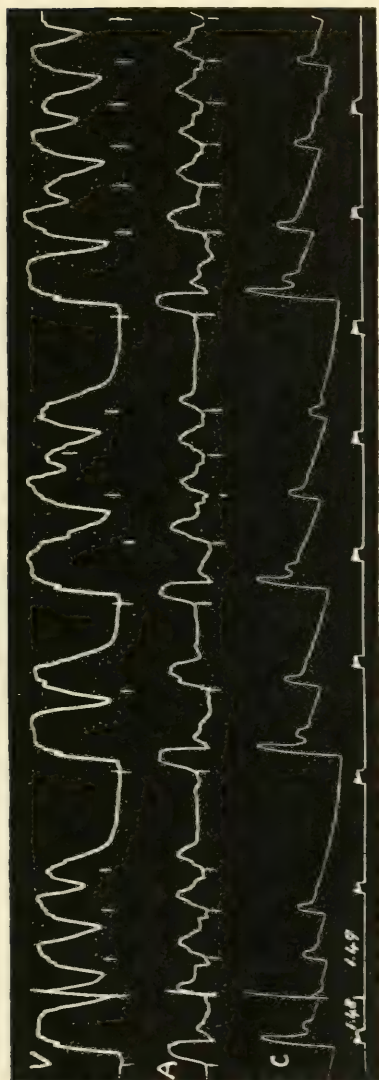


Fig. 2. Dog K; 1.48 1.49. Onset of fourth paroxysm. The lettering is the same as in Fig. 1. One beat of the normal rhythm is shown. Following the stops are three ventricular extrasystoles, each retrograde to the auricle. Only two of them effected the carotid pressure. A long pause follows, in the auricle somewhat less than 1 sec., an I exactly equivalent in length to a single As As interval of the preceding normal rhythm (only one beat of the normal rhythm is shown). This is followed by a response of ventricle to auricle, an extrasystole retrograde to the auricle, and a shortened pause with a second response of ventricle to auricle. Four retrograde extrasystoles succeed this response, of which only the second and fourth effect carotid pressure. The pause following these beats is again exactly equal to a single As As interval of the preceding normal rhythm. It is again succeeded by a response of ventricle to auricle, and from this point on beats arising in the ventricle and causing regular auricular contraction occur. The last beats shown are continued into the true paroxysm in the original tracing; a paroxysm lasting $\frac{1}{2}$ minute. The alternation which was clearly marked during the paroxysm, is shown in the ventricular and carotid tracings. The rate of the paroxysm was 157; the Vs As interval 0.12 sec.; the Vs As interval of the retrograde beats shown is about 0.16 sec.

TABLE II.
TABLE OF PAROXYSMS.

| RHYTHM PRECEDING PAROXYSM. | | | | PAROXYSM. | | | | | | | | | |
|----------------------------|-----------------|----------------|-------|-----------------|------------------------|---------|--------------|-----------------|---------------|--------------------|----------------------------|--------|---------------------|
| Dog. | Atrial Paroxysm | Irregularity. | Rate. | As. V's in sec. | Pre-oxysm. V's in sec. | V rate. | A rate. | V's-A's in sec. | Alternation | Length of | Termination in | | |
| C. | L.C. | Successive VEs | 92 | 0.10 | 5 m. | 165 | 90 | — | marked slight | 1 m. | N.R., with successive VEs. | | |
| | | | 95 | 0.11 | 2 m. | 153 | —153 | 0.28 | | | | | |
| C. | R.C. | " | 105 | 0.12 | 2 m. | 170 | 170 | 0.13 | absent | 31 m. | Fibrillation of V. | | |
| | | | | | | 180 | 180 | 0.14 | | | | | |
| | | | | | | 210 | 210 | 0.15 | slight | | | | |
| | | | | | | 180 | —180 | — | marked | | | | |
| H. | R.C. | AEs; VEs, etc. | 48 | 0.12 | 2 m. | 228 | 228 | 0.16 | 35 m. | Fibrillation of V. | | | |
| | | | | | | 375 | fibrillation | — | | | | | |
| | | | | | | 180 | " | — | | | | | |
| | | | | | | 183 | 183 | 0.13 | | | marked | | |
| I. | I. | VEs; REs | 152 | 0.11 | 5 m. | 140 | 140 | 0.15 | marked | 15 m. | Fibrillation of V. | | |
| | | | | | | 206 | 103 | — | | | | | |
| | | | | | | 224 | 156 (irreg.) | — | marked | | | | |
| | | | | | | 312 | " | — | marked | | | | |
| | | | | | | 289 | " | — | marked | | | | |
| | | | | | | 203 | 203 | — | marked | | | | |
| J. | J. | VEs; REs | 160 | 0.09 | $\frac{1}{2}$ m. | 300 | 300 (irreg.) | — | marked | 1 m. | N.R. | | |
| | | | | | | 272 | 136 | 0.11 | | | | marked | |
| | | | | | | 192 | 192 | 0.15 | absent | | | | |
| | | | | | | 234 | 156 | — | absent | | | | |
| | | | | | | 193 | 193 | 0.11 | absent | | | 29 m. | Experiment stopped. |
| | | | | | | 142 | 142 | 0.13 | absent | | | | |
| | | | | | | 270 | 135 | 0.13 | marked | | | | |

| E. | 1 | 2 | 3 | 4 | VEs | 91 | 0.09 | 10 m. | 206 | 103 | 0.14 | marked | 1 m. |
|------------|---|---|---|---|------------------------------|-------|-------|------------------|------------------|---------------|----------|-------------------|-----------------------|
| | | | | | | | | | | | | | |
| K. | | | | | .. | 87 | 0.11 | $\frac{1}{2}$ m. | 157 | 157 | 0.15 | absent | 1 m. |
| | | | | | VEs & REs | 70 | 0.10 | 1 m. | 234 | 117 | 0.15 | marked | 2 m. |
| | | | | | REs | 96 | 0.12 | $\frac{1}{2}$ m. | 192 | — | variable | marked | 1 m. |
| | | | | | | | | | 157 | 157 | 0.12 | marked | 1 m. |
| M. | | | | | VEs & REs | 119 | 0.10 | 1 m. | 220 | 110 | 0.12 | marked | 2 m. |
| | | | | | VEs & REs | 91 | 0.10 | 3 m. | 174 | 174 | 0.14 | slight | 4 m. |
| | | | | | VEs & REs | 107 | 0.11 | 1 m. | 156 | 156 | 0.14 | slight | 1 m. |
| O. | | | | | VEs | 168 | 0.08 | 4 m. | 356 | 165 | — | extremo | |
| | | | | | | | | | 356 | fibillation | — | marked | |
| | | | | | | | | | 345 | ? fibillation | — | marked | |
| | | | | | | | | | 340 | or response | — | absent | |
| P. | | | | | VEs | 158 | 0.07 | 1 m. | 310 | 77.5 | ? | extremo | 2 $\frac{1}{2}$ m. |
| | | | | | | | | | 374 | 169 | — | extremo | |
| | | | | | | | | | 380 | 190 | 0.12 | marked | 2 m. |
| | | | | | | | | | 150 (responding) | variable | — | marked | |
| R. | | | | | Slow retrograde mixed rhythm | (15) | — | 1 m. | 380 | 147 | — | extremo | 6 m. |
| | | | | | | | | | 294 | fibillation | — | absent | |
| | | | | | | | | | 405 | fibillation | — | (pulse irregular) | |
| | | | | | VEs | 108 | 0.08 | 12 m. | 260 | fibillation | — | absent | a few sec. |
| R. | | | | | | 180 | 0.08 | 1 m. | 257 | ? fibillation | — | absent | — 1 m. |
| | | | | | | 168 | 0.08 | 13 m. | 202 | ? fibillation | — | absent | a few sec. |
| | | | | | VEs | 164 | 0.09 | 2 m. | 271 | 161 | — | marked | a few sec. |
| | | | | | VEs | 168 | 0.10 | $\frac{1}{2}$ m. | 238 | 161 | — | marked | a few sec. |
| | | | | | VEs | 161 | 0.08 | $\frac{1}{2}$ m. | 206 | 165 | — | absent | 6 m. |
| | | | | | | | | | 235 | fibillation | — | absent | 3 sec. |
| | | | | | VEs | 157 | 0.10 | 1 m. | 348 | 174 | 0.11 | extremo | N.R., with VEs & REs. |
| | | | | | | | | | 280 | 140 | 0.12 | marked | |
| R. | | | | | | | | | 320 | 160 | — | slight | 14 m. |
| | | | | | | | | | 264 | 132 | 0.10 | — | |
| | | | | | | | | | 251 | 152 | — | — | |
| | | | | | | | | | 225 | fibillation | — | — | |
| R. | | | | | VEs & REs | 142 | 0.12 | 1 m. | 420 | 70 (approx.) | — | slight | less than 1 m. |
| | | | | | | | | | | | 0.139 | — | |
| Averages = | | | | | | 126.8 | 0.095 | | 253.3 | | | | |

As = auricular systole; Vs = ventricular systole; V = ventricular; A = auricular; L.C. = left coronary; R.C. = right coronary;
 VEs = ventricular extrasystole; AEs = auricular extrasystole; REs = retrograde extrasystole; N.R. = normal rhythm.

* This figure is excluded from the average.

the shape and length of the beats, and as regards the length of the Vs-As intervals. The curve may be interpreted as showing portions of three separate paroxysms, of which the first and second are transitory.

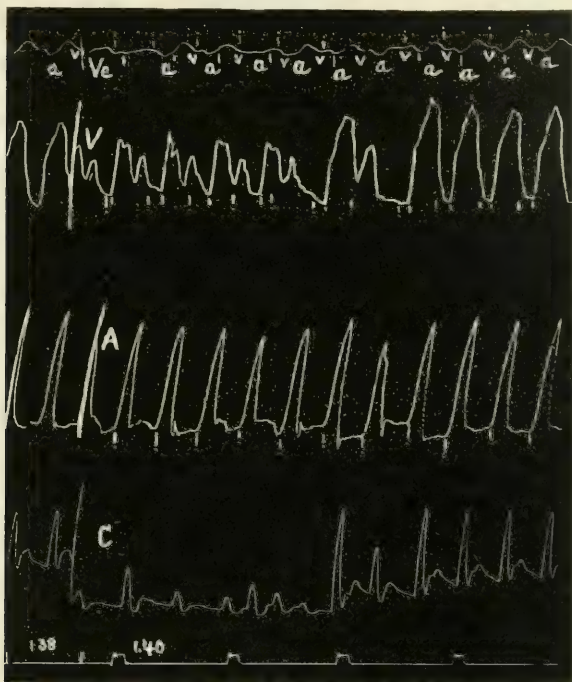


Fig. 3. Dog P; 1.38-1.40. Onset of fourth paroxysm. The auricular rate is approximately 164 throughout, that is to say, auricle responds to sinus throughout. To the left is the end of the normal rhythm. To the right is the paroxysm. The auricle and ventricle beat independently, the latter at approximately 271 with marked alternation. The alternation and dissociation, in combination, produce a very complex carotid curve. The ventricular paroxysm passes into response of ventricle to auricle. The regular *a* waves are clearly seen in the jugular curve, *Ve*. As opposed to the remaining curves, the curve of venous volume is inverted, it is marked above with points corresponding to *As*, and below to points synchronous with *Vs*.

The onset with the response of the auricle to each beat of the ventricle is by no means invariable, and the absence of this reaction is especially seen when the rate of the original sinus rhythm is rapid. In such cases the

auricle may proceed at its former rate, and coordination between the two chambers is completely lost. This type of curve is exemplified in Figs. 3 and 4. The complete dissociation which exists in these instances may terminate in one of three distinct ways. The auricle may pass into a state of fibrillation (Fig. 4). The ventricular rhythm may cease with a return to the original sequence (Fig. 3). Finally, the auricle may become irregular as a consequence of, at first, occasional, and eventually frequent or continuous responses to the ventricle.

At this stage it will be found convenient to note the mode in which the rhythm changes when fibrillation of the auricle is present. An examination of the other phenomena of the paroxysm may be proceeded with subsequently.

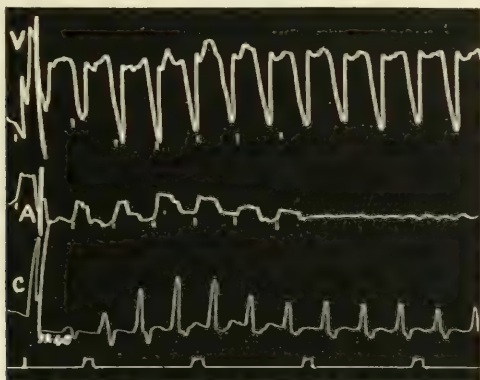


Fig. 4. Dog O: 12.36-12.40. Onset of first paroxysm. To the left of the stops a beat of the normal rhythm is shown. The rate of this rhythm was 168. The paroxysm commences with complete dissociation. The auricle continues to respond to the sinus at 160. The ventricular rate appears at first sight to be 178. The subsequent curve proved that alternation was present at this stage, and the real ventricular rate is 356, for each of the ventricular curves shown in reality consists of two beats. An indication of the alternation is seen in some of the carotid curves. The carotid curve shows a gradual waxing and waning of systolic pressure, according to the instants at which the auricular beats fall. The auricle passes into fibrillation after six beats.

AURICULAR FIBRILLATION DURING THE PAROXYSMS.

A flickering or tremulous movement of the auricle has been noticed upon many occasions. When it occurs, it manifests itself, as a rule, at or within a few seconds of the commencement of the tachycardia (as in Dog H, O, and P). Under these circumstances it appears to be the result of the impulses showered upon it from above and below. It may be regarded as an expression

of trembling indecision, or as a complex response to a superabundance of stimuli reaching it on more than one side. Usually the eventual result is the acceptance by the auricle of the more urgent demands of the ventricle. The curve described is small in amplitude and irregular in outline, or may show no other indication of movement than a slight transmitted pull from the ventricle. But it is often difficult to satisfy oneself that true fibrillation is present, in the absence of knowledge of what constitutes true fibrillary twitching. A marked incoordination of its fibres may be present, yet this condition may pass imperceptibly into undisturbed and regular beats.

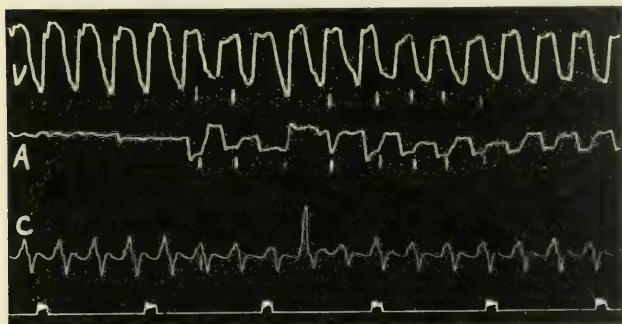


Fig. 5. Dog O; 12.51. Taken during the second paroxysm. The curve shows the auricle at first in fibrillation, and later responding to the ventricle. As in the last figure the stimulus production in the ventricle is in reality double the apparent rhythm (actual rate about 380, apparent rate about 190). The events occurring between Figs. 4 and 5 are contained in the protocol. The final rate of the ventricle in this experiment was 405 (Fig. 6).

Auricular fibrillation was also met with on another occasion (Fig. 6), namely, when the ventricular rate rose to 405.

When established it terminates in one of three ways:—

- (1) As stated above, it ends in the auricle responding to the ventricle (Fig. 5);
- (2) It passes into auricular response to stimulus production at a higher level, while the paroxysm ends, and the ventricle responds to the auricle;
- (3) Ventricular fibrillation ensues. In such cases, so soon as ventricular fibrillation is established, the auricle tends to respond once more to impulses created at a higher level.

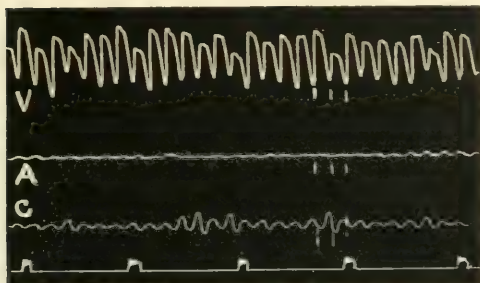


Fig. 6. Dog O; 12.58. Nearing the termination of the experiment. The ventricle is beating with a regular rhythm of 397. The auricle shows fibrillation. The small waves on the curve A are transmitted from the ventricle. The carotid curve is monocrotic.

DISSOCIATION AND HEART-BLOCK DURING THE PAROXYSMS.

With the onset of the new or paroxysmal rhythm, it sometimes happens that the auricle maintains its original rate. In such cases there is complete independence of two rhythms, which are individually regular (Figs. 3 and 4). It is generally brought about when the ventricular only slightly exceeds the auricular rate, that is to say, when the original auricular or sinus rhythm is unusually fast. It is probable that the absence of retrogression in these instances is largely due to this enhanced rate, it may also depend upon the presence of an exceptional hindrance to the backward passage of the beats. As Trendelenburg and others have shown, retrograde beats are called forth most readily at a time when the heart beat is slow. The presence of complete dissociation where the rate of ventricle but slightly exceeds that of the auricle, gives rise to a characteristic periodicity in the carotid tracing, a waxing and waning of the curve which is well marked for a short distance in Fig. 4. It is dependent upon the instant, in relation to ventricular systole, at which the auricle contracts (Cushny).

Partial heart-block during a paroxysm occurs spontaneously and is very frequent. It is produced by great acceleration of the ventricular rhythm. Thus, in Table II, 2:1 heart-block is shown to have occurred when the rate of ventricular contraction was counted at 206, 272, 270, 206, 234, 220, 380, 294, 348, 280, 320, and 264. The 4:1 ratio is of rarer occurrence. It is illustrated in Fig. 8. Examples of response to each ventricular beat were met with at the following rates:—153, 170, 180, 210, 180, 228, 183, 140, 203, 192, 193, 142, 157, 192, 157, 174, and 156. The halving of the auricular rhythm appears to take place when the ventricular rhythm rises above 220, or thereabout.

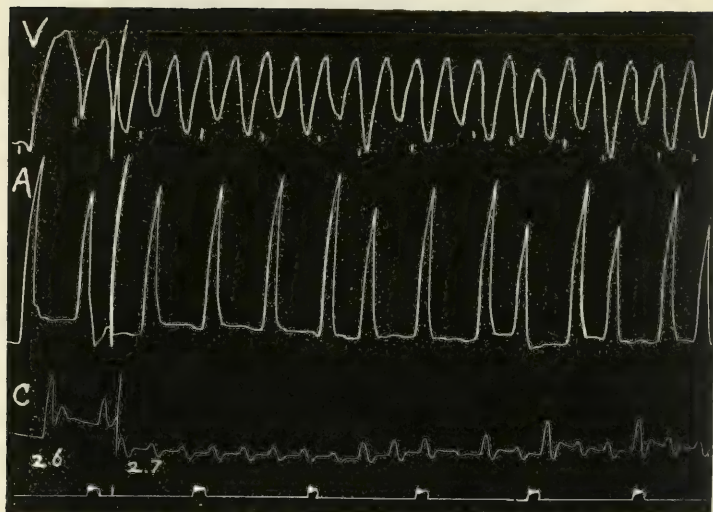


Fig. 7. Dog M; 2.6-2.7. The onset of the first paroxysm. To the left is the normal rhythm, interrupted by a ventricular extrasystole. To the right is a ventricular paroxysm at approximately 220. Alternation is well seen in the ventricular curve, but is less marked in the carotid. At first the auricle responds to every second beat, and later to 2 in 3. With the 2:3 rhythm a periodic variation in the carotid tracing and a variation in Vs-As interval are seen.

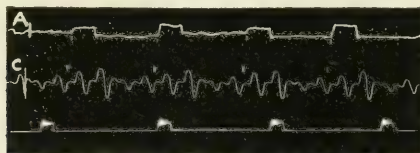


Fig. 8. Dog O; 12.42. Two minutes after the onset of the first paroxysm. Auricular and carotid curves are shown. Reversed heart-block (4:1) is present. The effect of the auricular beat upon the carotid tracing is clearly shown. The ventricular rate is 310. As in several of the figures taken from this experiment, the auricular beat is unduly prolonged (cp. Figs. 4 and 5); it is probable that we have to do in such cases with a special action of the auricle verging on fibrillation.

Examples of 2:1 reversed heart-block are given in Figs. 5, 7, and 11 (in two of which, Figs. 5 and 11, alternation of the ventricle is present.

Fig. 5 does not demonstrate the alternation, but its presence was quite clear from an examination of the continuation of the same tracing)*. In Fig. 7 a 2:1, 1:1 alternating ratio is shown, in which there is a variation of the Vs-As interval according to the time allowed for recovery. The size of the auricular contraction is also affected by the same circumstance.

Both in this curve, and in that shown in Fig. 8, an example of 4:1 ratio, the effect of the auricular beats upon the carotid curve is very marked. The variation in the pulse curve produced by the auricular beats is of considerable clinical importance, for it is invariable, and it leads to the conclusion that in the human subject, where the radial curve is composed of beats of constant size, the sequence of contraction in auricle and ventricle, if there be a sequence, is constant. Further, it may be suggested, that where the height of the pulse beats are not consistent with the preceding pauses some degree of independence of auricle and ventricle may be present.

In the further consideration of heart-block as it occurs during the paroxysms, the occasional missed response of the auricle in an otherwise regular rhythm must be mentioned.

Vagal stimulation may give rise to heart-block *de novo* in reversed rhythm, or may increase the grade of heart-block originally present. Such effects may be explained in the case of a retrograde rhythm, either as a result of the vagal action direct upon the auricle, or as a consequence of an alteration produced in the conducting power of the auriculo-ventricular bundle.

THE EFFECT OF VAGAL STIMULATION AFTER THE ONSET OF THE PAROXYSM.

Full details of the consequences of vagal stimulation during the normal rhythm and while the paroxysms prevailed are given in the accompanying table (Table III).

The strength of the faradic current employed was selected physiologically in the majority of instances. That strength of current was employed which produced marked slowing or temporary standstill of the heart before the commencement of the paroxysm. Where stronger or weaker currents were employed the fact is stated.

It will be seen that, in most instances, vagal stimulation results in missed auricular contractions. The beats may be dropped regularly, with the production of a definite reversed heart-block ratio, or the increase of a pre-existing ratio, or it may be irregular. *In none of these instances is the rhythm of the ventricle affected.* In Fig. 9, three auricular beats are dropped, and the response of the large escaped beat of the auricle succeeds a marked

* In most instances, but not in all, when this 2:1 rhythm is present, and when the ventricle alternates, the auricle responds to the larger ventricular beat.

TABLE III.—EFFECT OF VAGUS STIMULATION SUBSEQUENT TO LIGATION OF CORONARY ARTERIES.

| Dog. | DURING THE NORMAL RHYTHM PRECEDING PAROXYSM. | | DURING THE PAROXYSM. | |
|--------|--|--|----------------------|--|
| | | | | |
| C. . . | { | 1). Slowing of whole heart with synchronous escape of auricle and ventricle. | { | 1). Reversed heart-block, 4 : 1. Ventricle unaffected. |
| | | 2). 2 : 1 heart-block. | | 2). Reversed heart-block, 2 : 1. Ventricle unaffected. |
| G. . . | { | 1). Slowing of whole heart with escape of auricle. | { | 1). Reversed heart-block, 4 : 1. Ventricle unaffected. |
| | | 2 and 3). Slowing of whole heart with staircase in force of auricular contraction on recovery. | | 2). Reversed heart-block, 2 : 1. Ventricle unaffected. |
| H. . . | { | 1). Slowing of whole heart with staircase in force of auricular contraction on recovery. | { | 1). Reversed heart-block, 4 : 1. Ventricle unaffected. |
| | | | | 2). Auricle stops for 5, 3, and 7 beats. Ventricle unaffected. |
| | { | | { | 3). Auricle stops for 4 and 10 beats. Ventricle unaffected. |
| | | | | 4). Reversed heart-block, 4 : 1. Ventricle unaffected. |
| | { | | { | 5). Reversed heart-block, 2 : 1 (weaker). Ventricle unaffected. |
| | | | | 6). Auricle stops for 15 beats (stronger). Ventricle unaffected. |
| I. . . | { | 1, 2, and 3). Slowing of whole heart with staircase in force of auricular contraction on recovery. | { | 1 and 2). No effect. |
| | | 4). Slowing of whole heart with separate escape of A and V. | | 3). (Stronger). Ventricular pause of 1·2 sec. ; auricular pause, 1·1 sec.,. Reappearance of normal rhythm. |
| J. . . | { | 1). Slowing of whole heart with single dropped ventricular beat. | { | 1). Auricle stops for 5 beats, followed by reversed heart-block, 2 : 1. Ventricle unaffected. |
| | | | | 2). Marked auricular slowing. Ventricle unaffected. |
| | { | | { | 3). Reversed heart-block. Ventricle unaffected. |
| | | | | 4). Marked slowing of A. Ventricle unaffected. |
| K. . . | { | | { | 1). Pause of ventricle for 1·5 sec. ; auricular pause, 1·3 sec.,. Return to normal rhythm. |
| | | | | 2). Pause of ventricle and auricle. Return to normal rhythm. |
| M. . . | { | 1). Whole heart stops for 3 sec.,. | { | 1). Return to normal rhythm. |
| | | | | 2). Dropping out of auricular beats (Fig. 9). |
| O. . . | { | 1). Whole heart markedly slowed. | { | 3). Return to normal rhythm (Fig. 10). |
| | | | | 1). Auricle drops 1, 3, 2, 4, 2, and 2 beats. Ventricle unaffected. |
| | { | | { | 2). 3 : 2 reversed heart-block, converted to 4 : 1. |
| | | | | 3). Auricular beats dropped. Ventricle unaffected. |
| P. . . | { | 1). Whole heart stops for 3 sec., staircase of auricle on recovery. | { | 1). 2 : 1 reversed heart-block, converted to 4 : 1. |
| | | 2). Whole heart stops for 3 sec., staircase of auricle on recovery. | | 2). Auricle misses 5, 3, 5, and 5 beats. Ventricle unaffected. |
| | { | 3). Whole heart stops for 3 sec., staircase of auricle on recovery, with alternation of auricle. | { | 3). Auricle misses 5, 3, 4, and 5 beats. Ventricle unaffected. |
| | | | | 4). Auricle misses 3, 2, 3, 4, 5, and 3 beats. Ventricle unaffected. |
| | { | | { | 5). Auricle misses 4, 3, 3, and 3 beats. Ventricle unaffected. |
| | | | | |

prolongation of the Vs-As interval. The figure also shows a return to the normal or sinus rhythm, later in the experiment. The effect of the large auricular beat upon the radial pulse should be noted.

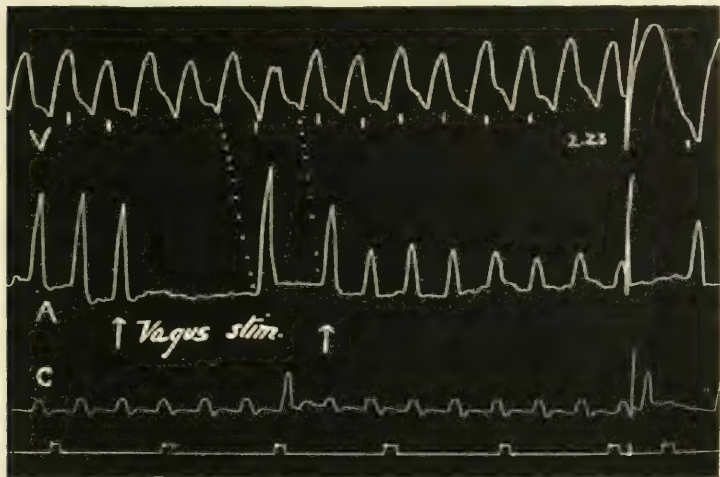


Fig. 9. Dog M: 2.23-2.24. The figure shows the falling out of three auricular beats as a result of vagus stimulation. The Vs-As interval of the first auricular response is greatly prolonged. The effect of the large auricular beat upon the carotid curve is well marked. The offset of the paroxysm to the normal rhythm, a small portion of which is shown, was spontaneous.

In three out of the eight experiments (Dogs I, K, and M) excitation of the vagus produced a different effect. The whole heart stood still for a variable time, and with its escape, returned to the normal rhythm. In the figure (Fig. 10), the standstill of the auricle chanced to correspond to two previous auricular cycles, but, as a rule, this was not the case. The rhythm following the standstill is interrupted by a single retrograde extrasystole. It is questionable whether the first ventricular beat which follows the stimulation is a response to the auricle or not, for the As-Vs interval is reduced.

The occasional and complete standstill of the heart does not affect the arguments subsequently employed in these pages, but it is of interest in that, assuming the origin of the paroxysmal rhythm in the ventricle, it demonstrates the direct control of the ventricle by the vagus in 30 per cent, at least of the animals employed.

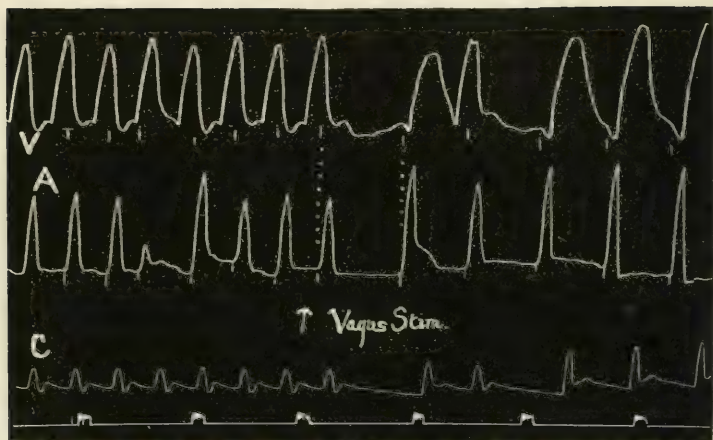


Fig. 10. Dog M: 2.36. The curve shows an occasional effect of vagal stimulation during a paroxysm. In the early part of the curve a spontaneous auricular extrasystole occurs. It does not effect the ventricular rhythm, and has a full compensatory pause. Stimulation of the vagus stops auricle and ventricle, proving the latter to be subject to vagal control. The normal rhythm is resumed after an auricular pause, which is equivalent to two previous auricular cycles, but this is probably accidental. The slow rhythm is interrupted by a single ventricular extrasystole which is probably retrograde.

ALTERNATION OF THE AURICLE DURING THE PAROXYSMS.

Alternation of the ventricle is of common occurrence during the paroxysms, but the many interesting facts observed in this connection must be left for a future communication.

Certain points noted in connection with alternation may be briefly outlined. Alternation may be present in auricle as well as ventricle, and the alternation in one and the other may not coincide from beat to beat. Alternation in the ventricle may or may not coincide with alternation in the carotid. It is impossible to state from the ventricular curve to what extent alternation may be expected in the carotid. This is clearly shown by Fig. 11. The presence of extreme alternation may render its detection difficult, and as it gradually disappears it may lead to an apparent doubling of the pre-existing ventricular rate. Curious and sudden alterations in the amount of alternation may occur. When a 2:1 reversed heart-block is present, and the ventricle shows marked alternation, the auricle usually responds to the more forcible ventricular beat. Alternation is shown in Figs. 2, 3, 4, 5, 7, 9, 10, and 11.

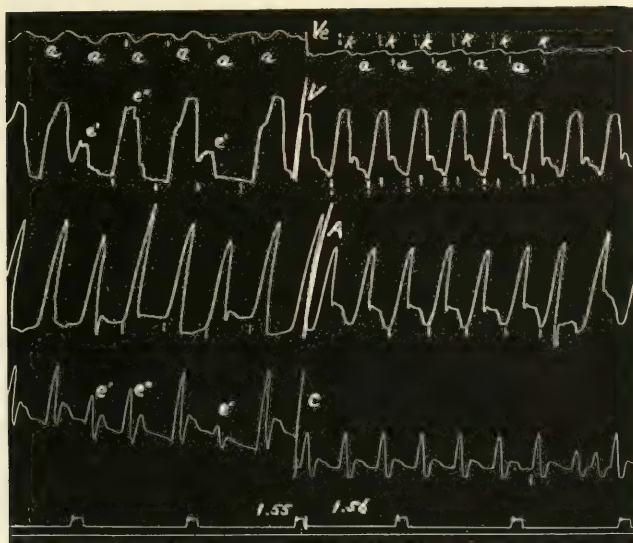


Fig. 11. Dog P: 1.55-1.56. V_e =curve of volume of external jugular vein. The curve is inverted, as in Fig. 3. The figure shows the onset of the eighth paroxysm. To the left is the sinus rhythm, interrupted by three extrasystoles of the ventricle. The auricle beats regularly at 157. The venous curve shows the a waves to be regular, and slightly delayed. To the right is the commencing paroxysm. The auricle is beating at 177. The stimulus production in the ventricle is at the rate 354. Extreme alternation is present, but the weaker beats are only just perceptible. The sudden change in the carotid curve is possibly the result of the preceding anomalous auricular contraction. At the end of the tracing one of the stronger beats is reduced in size in the carotid curve, and is followed by a beat of equal strength, yet the tracing of the ventricle shows no change. The curves passed gradually to those in which alternation was easily distinguishable in ventricular and carotid tracings. The venous curve shows waves marked k and a . The venous curve is marked with points which correspond to As below and Vs above. As in this figure the paroxysm is usually accompanied by a considerable fall of blood pressure.

VENOUS CURVES OBTAINED DURING THE PAROXYSMS.

Curves of venous volume were obtained in many of the experiments. In most of the figures they have not been included. They are shown in Fig. 3 and in Fig. 11. They are inverted. In the former (Fig. 3) a short curve is shown to the left of the stops in which a and v waves are well marked. In the succeeding paroxysm, in which complete dissociation is present, the combination of a and v waves are clearly indicated. With the establishment of the normal rhythm a and v waves appear again. In Fig. 11, taken from

the same animal, similar curves are shown to the left of the stops. The ventricular extrasystoles do not interfere with the regular *a* waves. To the right of the stops, auricle and ventricle are contracting simultaneously, and as ventricle precedes auricle, so a wave marked *k* precedes the wave *a*. The alternate beats of the ventricle are too feeble to affect the jugular curve. The tracing is of chief interest in that all waves fall within the period of ventricular systole, as in clinical nodal rhythm; further, they bear at least a superficial resemblance to the clinical tracings, in that two waves, separated by a depression, are present.

THE TERMINATION OF THE PAROXYSMS.

The paroxysms may terminate in several ways. Usually there is an abrupt return to the normal rhythm (Fig. 10)*, in some instances they pass into fibrillation of the ventricle.

When a change takes place from tachycardia to the original sinus rhythm, a well-marked pause occurs. It is necessarily longer in the ventricular curve than in the auricular, for the first beat of the normal rhythm is a response of the ventricle to the auricle. The pause varies in length, and no constant relationship exists between it and the preceding or subsequent rhythm†. In this respect it is precisely similar to the pause which is seen at the termination of paroxysms met with in patients the subject of paroxysmal tachycardia (for an account of the pause in such a case see Lewis, this *Journal*, Vol. I, p. 43). A similar pause has been recorded by Rihl⁷ in an experiment in which auricular tachycardia was produced by rapid interrupted stimulation of the auricle. Presumably the pause represents the time taken for the building up of the impulse which calls forth the first beat of the normal rhythm, but there seems to be no rational explanation of its variation in length, or of the frequent lack of harmony between it and the spacing of the beats which are adjacent to it. It is probable that it will be better understood when the factors inducing the change from one rate to the other are found. Its length and variability are of importance in certain instances in excluding the possible presence of sino-auricular block; and it may be that in the future it will be found to constitute a valuable sign in the recognition of clinical paroxysms, which are purely myocardial in origin.

When the paroxysm ends in ventricular fibrillation, the rate of contraction of the lower chamber is generally very rapid. Tracings of the change from one to the other are extremely difficult to interpret. It is impossible to state where the ventricular rhythm ends and the fibrillation begins, the

* As the number of figures is already large, a duplicate curve showing the spontaneous termination of a long paroxysm in the normal sequence is not published.

† Where only a few retrograde beats occur before the pause (as in Fig. 2), the auricular pause may be equal to a single As-As interval of the preceding rhythm. Where the pause comes after a long paroxysm, no such relationship, and no constant relationship to the succeeding rhythm can be established.

transition point cannot be fixed by the most careful inspection of the heart. Precisely the same observation applies to the galvanometer curves, the fast paroxysmal curves change imperceptibly into those which characterise fibrillation. The galvanometer curve of fibrillation which Kahn² has published is a typical one, it consists of long waves of surprising excursion arranged in an irregular fashion. The curve is by no means that which would be anticipated from our knowledge of the visible movements. Levers attached to the ventricle during fibrillation show slight irregular and comparatively slow oscillations, and the oscillations of the mechanically traced curve correspond to the waves of the electric curves (cp. Protocol of Dog R). A general underlying movement of the heart wall, apart from the fibrillary twitching, must consequently exist when the ventricle passes into this state.*

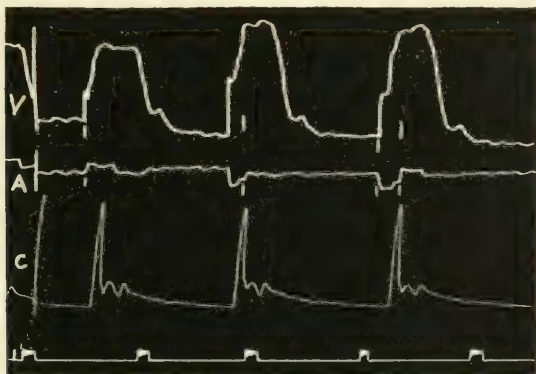


Fig. 12. Dog O; 12.53. (Taken between Figs. 5 and 6). The curve is an example of a curious slow rhythm, into which the paroxysm passed on two occasions in this experiment. The rhythm, of which three (possibly six) beats are shown, presented a mixture of cycles, in some of which auricle and ventricle contracted simultaneously, in others auricle preceded ventricle, and in yet others ventricle preceded auricle. Neither auricle nor ventricle were exactly regular for two beats together. The last two auricular beats in the figure are complicated by the contraction of the ventricle.

In one animal (Dog O) the paroxysm ended on two occasions in a slow rhythm of a peculiar nature (Fig. 12). It consisted of a slow and irregular contraction of the ventricle, and of a similar and generally equally irregular

* Galvanometer curves during auricular fibrillation have since been obtained; the auricular movements, whether coarse or fine, yield currents approximately commensurate with such movements. The "rhythme affolé," of the ventricle, which accompanies it, produces the curve expected; each ventricular beat is accompanied by R and T waves, similar to those of the preceding and succeeding normal beats. While the abnormal rhythm is present, therefore, the impulses which give rise to it reach the ventricle along the usual path.

action of the auricle. Some of the auricular beats could be interpreted as retrograde responses, others (which are not shown in the figure) of more occasional occurrence, as responses of the ventricle to auricle. A few contractions, as, for example, the first of those seen in the figure, demonstrate simultaneous systole of auricle and ventricle. The nature of this rhythm is quite obscure. It could not be produced by stimulation of the vagus during the paroxysms. It appears to bear some relationship to the rhythm described by Mackenzie in the first number of this *Journal* under the title "Nodal bradycardia."

When the paroxysm ceases at the re-establishment of the normal rhythm certain irregularities are noticed which have been described already. They take, almost always, the form of ventricular extrasystoles. They are more commonly retrograde than those which precede the tachycardia. An example of regularly occurring retrograde beats is given in Fig. 13. A single retrograde contraction is also depicted at the termination of a paroxysm under vagal stimulation in Fig. 10.

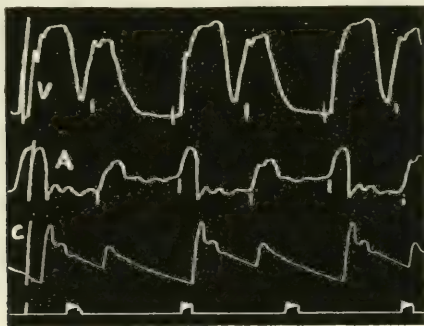


Fig. 13. Dog K: 1.52. The curve was taken 3 minutes after the cessation of a paroxysm. It shows bigeminy of auricle and ventricle, due to retrograde extrasystoles. The bigeminy is less marked in the auricle than in the ventricle, by the sum of the As-Vs and Vs-As intervals.

Before passing to a general discussion of the nature of the abnormal mechanisms of cardiac action described in the foregoing pages, a table is given in which a general outline of the more striking events which have been recorded is given. (On the left of the table the rhythm preceding the paroxysm is stated; bracketted to it are the conditions of paroxysm into which it may pass (V.P. = ventricular paroxysm); bracketted to each of these again, are the events which may follow; and so the table continues until the normal rhythm or ventricular fibrillation is established. To the right of each line the particular paroxysm or paroxysms, sketched in this way, are indicated.

Thus, "Normal rhythm with or without ventricular or retrograde extrasystoles" may give place to one of three conditions, and each of these in turn may terminate in two or more ways.)

| | | | |
|---|-------------------------------|---|---|
| 1. Normal rhythm with or without ventricular or retrograde extrasystoles. | 1. V.P. ; A responding. | 1. V fibrillates (Dog P, paroxysm 7). | |
| | | 2. Normal rhythm (Dog K, 1, 2, and 4 ; Dog M, 1, 2, and 3). | |
| | 2. V.P. ; A fibrillates. | 1. V.P. ; A responds. | 1. V fibrillates (Dog H) ; (Dog P, 1, 2, and 3). |
| | | 2. Normal rhythm. | |
| | 3. V.P. ; A at previous rate. | 1. V.P. ; A responds. | 1. Normal rhythm (Dog C, 2). |
| | | | 2. V fibrillates (Dog G and J). |
| | | 2. V.P. ; A fibrillates. | 1. Normal rhythm (Dog P, 6). |
| | | | 2. V.P. ; A responds. |
| | | 3. Normal rhythm. (Dog C, 1, and Dog P, 4 and 5). | 1. Slow abnormal rhythm (Dog O, 1 and 2) (Fig. 12). |
| 2. Slow abnormal rhythm (Fig. 12). | 1. V.P. ; A responds. | 1. V.P. ; A fibrillates. | 1. V fibrillates (Dog O, 3). |
| | 2. Normal rhythm (Dog O, 1) | | |

THE GALVANOMETER CURVES OF THE EXTRASYSTOLES AND
OF THE BEATS OF THE PAROXYSMS.

The curves taken with the galvanometer, with simultaneous records of auricular and ventricular movements, allow of a very accurate analysis of the heart's mechanism, from time to time. In the interpretation of the curves it must not be forgotten that the current was led from the limbs, with the chest wall open, and that a large portion of the ventricular musculature was in a state of partial or complete inactivity. Therefore, it cannot be expected that the curves will be exact duplicates of what are now regarded as normal

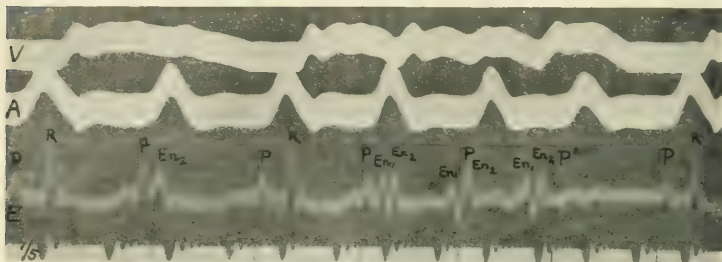


Fig. 14. Dog R; 12.17. E is the galvanometer curve. From first to last the curve shows, response of ventricle R, to auricle P; ventricular extrasystole consisting of two waves (first and second base negative waves) upon the first of which the auricular wave is superimposed; response of ventricle to auricle; ventricular extrasystole with P falling slightly before it; ventricular extrasystole with P falling on En_2 ; retrograde extrasystole with the auricular wave small and inverted; response of ventricle to auricle. The curve demonstrates the anomalous character of the electric curve of a retrograde auricular response. Corresponding points are exactly vertical over each other.

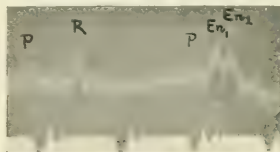


Fig. 15. Dog R; 12.40. The electric curve, which shows a normal response and an extrasystole, is given for comparison with the next figure.

curves: yet, on the whole, they show a very close approximation to them*. In all the normal curves shown (Figs. 14 and 15) the P wave of the auricle,

* The cutting out of large areas of the musculature by obstructing the blood supply, should ultimately prove of value in arriving at conclusions as to the manner in which the normal electrocardiogram is produced.

and the first or R wave of the ventricle stand out clearly. In the figures, ventricular extrasystoles are also represented. They are all alike, and consist of two peaks (En_1 and En_2), displacements in a direction indicating negativity of the basal end of the ventricle. The size of the peaks varies, for here and there the P waves are superimposed upon them. Ventricular extrasystoles are shown, to which the auricular contractions bear varying relationships. Thus, P is illustrated as falling directly before the extra contraction, or coinciding with En_1 or En_2 . In other curves the P wave fell after the extrasystolic curve*.

In Fig. 14 a row of three extrasystoles is seen, of which the third or last has affected the auricular rhythm. The point at which the retrograde auricular beat has arisen is represented in the galvanometer curve by a slight depression. *The normal P wave is completely absent.* Such was the case † wherever premature beats of the auricle, which could be interpreted as retrograde beats, took place. The atypical auricular wave, which was anticipated in a previous communication, is explained if we assume that the auricle contracts from below upwards, and if we regard the galvanometer curve as the expression of the direction of contraction in the heart. The observation is of importance in consideration of the electrocardiographic curves in instances of so-called nodal rhythm, or *pulsus irregularis perpetuus*, as it occurs in man. In these curves all sign of P waves is absent, but it is obvious that on this account we have no right to assume that the auricle is inactive. A further analysis of the phenomena would be of considerable value in interpreting clinical irregularities in which simultaneous contraction of auricle and ventricle is suspected.‡

The curves of the beats of the paroxysm itself are given in Fig. 16, and a comparison with the curves representing extrasystoles interrupting the normal rhythm shows their close similarity to these. Each consists of two peaks, which have been marked En_1 and En_2 respectively. The ventricular curve accompanying the electrocardiogram curve is obscure, but the beats of the auricle are distinct though weak. Two are shown in the figure; the remaining vibrations are transmitted from the ventricle. The occasional auricular contractions scarcely affect the galvanometer curve. There is, perhaps, a slight deepening of the depression between the peaks of adjacent ventricular systoles.

* The direction of the extrasystolic electric waves is opposed to the view adopted by Kraus and Nicolai⁷, that when the primary wave is in this direction, the right ventricle contributes more to the contraction than the left. We are dealing with an instance in which the right ventricle is probably less active than the left. That the beats have their origin in the right ventricle is a conclusion compatible with the statements of these authors, and with the present observations.

† The usual P wave was always absent, but at times the dip in the reverse direction was indistinct or absent.

‡ The writer has several galvanometer curves from patients in whom auricular extrasystoles were shown by polygraph tracings. These curves demonstrate conclusively the anomalous character of the auricular current, when it is due to an auricular contraction arising from an impulse other than a sinus impulse.

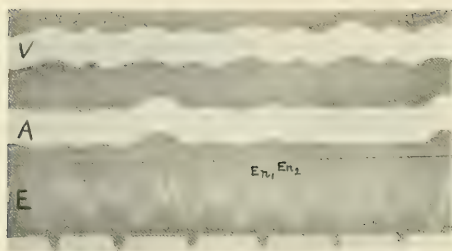


Fig. 16. Dog R; 12.56. The ventricular paroxysm is shown. The auricle is beating irregularly, but usually as 1 to 6. The auricular beats are retrograde responses, and tend to deepen the dips of the electrometer curve. The close resemblance of the individual beats to the extrasystole of Fig. 15 is apparent. The rate is 420 per minute. The curve passed directly to that of fibrillation, and it was impossible to say where one ended and the other began.

THE POINT AT WHICH THE PAROXYSMS HAVE THEIR ORIGIN.

For descriptive purposes it has been convenient to assume the origin of the tachycardia in the ventricle. Having now full access to the collected evidence, the proof of this assumption may be given.

The lesion produced is essentially one of the cardiac muscle, and, *a priori*, any abnormalities of rhythm resulting therefrom might be assigned to the altered conditions prevailing in the walls of the heart. There can be no question, in the case of the tachycardia considered, but that it arises independently of all central nervous control. Emphasis upon this point is necessary, for, in the past, sudden accelerations of cardiac rate have been too frequently attributed to altered innervation.

It remains to determine more accurately the exact locality in which the fast rhythm arises. We have seen that during the paroxysm the Vs-As interval shows constancy, and that various grades of heart-block may be established, either spontaneously or as a result of vagal stimulation, between the two chambers. As opposed to the usual condition the phenomenon is reversed, and it is the rate of the auricle which is reduced. Further, as a result of vagal irritation the auricle may be brought to a standstill; again, spontaneous fibrillation of the auricle may supervene. In all these conditions, if the paroxysm continues, as it usually does, the ventricular rhythm is absolutely unaffected. Moreover, while the ventricle beats at a paroxysmal rate the auricle may continue to respond to impulses arising at a higher level. Further, extrasystoles arising spontaneously in the auricle have a full compensatory pause, and do not affect the ventricular rhythm (Fig. 10 and explanatory remarks). The position is entirely reversed; for the

recognised characteristics of the ventricular extrasystole are portrayed in the auricle.

These facts are sufficient to demonstrate that the ventricular rhythm is independent of impulses received from the auricle. The new rhythm may arise in one of two conceivable ways. The ventricle may constitute the pace-maker of the heart, or it may respond to impulses arising from an independent area at a higher level, a focus from which it might be supposed that stimuli travel with greater facility to the ventricle than to the auricle. It is difficult to imagine, in the face of the evidence, in what part of the musculature such a focus might lie, and such a hypothesis is strongly negatived by the fact that the Vs-As interval during the paroxysm exceeds that of the As-Vs interval of the normal rhythm, and more particularly by the fact that the same relationship holds when a reversed rhythm is artificially excited by electric stimulation of the ventricle (Bayliss and Starling¹, and others*). The proposition, that the ventricle is the starting point of the new rhythm, is established by an examination of the muscular area damaged by ligation. When solely ventricular muscle is included in the lesion, extrasystoles of the ventricle alone are met with as the preliminary irregularity. In the case of the third experiment (Dog C), paroxysms in every way comparable to those obtained in the later experiments were recorded, and, in this instance, only a small portion of the ventricular musculature was thrown into a pathological condition. We may consequently conclude that the paroxysms arise in the ventricular walls. The evidence which has been given, is supported still further by the nature of the irregularities directly preceding and succeeding the paroxysm. The majority of the interruptions of the normal rhythm are recognised as extrasystoles of the ventricle, and it is highly probable that the paroxysm itself is nothing more than a succession of these beats: a conclusion which is warranted by the following facts. In most instances the paroxysm is foreshadowed by the occurrence of ventricular extrasystoles, which more and more tend to appear in groups. In many cases, the occurrence of several beats of this nature results in an interruption of the auricular rhythm, a result attributable to retrogression of the last spontaneous ventricular contraction. As the onset of the paroxysm approaches, the retrograde contractions increase in frequency, until eventually, with the establishment of the continuous intrinsic ventricular rhythm, the auricle responds regularly. The Vs-As interval of the single retrograde beat and the intervals during the paroxysm are compatible. The beats of a row of retrograde extrasystoles are frequently at the same rate as those of paroxysm, out of which they arise. Precisely similar arguments apply to the offset of the paroxysm, and the irregularities which interrupt the re-established normal rhythm. Finally, the galvanometer curves

* The figures for dogs given by Bayliss and Starling are: — As-Vs = 0.15-0.16 sec., and Vs-As = 0.19-0.22 sec.; the difference is in close agreement with the difference in the averages found in these experiments, namely 0.04 sec..

show a close resemblance between the extrasystolic contractions and those of the tachycardia itself. It may be concluded, therefore, that the paroxysm has its origin in the ventricular musculature, and that it is constituted by the establishment of a continuous succession of those beats which are usually designated extrasystoles.*

The level at which the new or ectopic rhythm arises in the ventricle is alone in doubt, and these observations throw insufficient light upon it. The similarity of the paroxysms, as they occur from one animal to the next in ligation of the right coronary artery, might suggest that some specially excitable focus exists in the right ventricular walls which is peculiarly susceptible to the disorder of nutrition accomplished by such ligation. The nature of the electric curve and the regularity of the rhythm are sufficient to demonstrate that the beats arise from a common and restricted area. That the ectopic rhythm probably arises in the damaged area is self-evident, and it is further probable that the impulses are formed, not in the centre of such an area, but at its border, where the muscle is still living, and where it is indifferently supplied with blood†. It may be supposed that the paroxysm is the result of a local and enhanced irritability, the offspring of anæmia.

THE RELATION OF EXPERIMENTAL TO CLINICAL OBSERVATIONS.

Paroxysmal tachycardia proper‡ occurs in man, and has received much careful study. It is now definitely known to exist in at least two forms. It may spring from a high, or may originate at a low, level of the heart. The actual points of origin have not been definitely determined in man, but the evidence leads to the belief that in one form the focus in question is certainly higher than the main mass of auricular tissue, and in the other form lower than the musculature of the auricle. The last-mentioned type may depend upon a reaction of the musculature to ectopic impulses having their birthplace in the node or other part of the conducting system, or in the

* If it is recognised that the paroxysm is constituted by frequent extrasystoles of a nature similar to those which precede its onset an interesting consideration arises. Taking, for instance, the paroxysm exemplified in Fig. 11, if it is assumed that extrasystolic and paroxysmal beats are originally of the same nature, the alternation which is commencing to manifest itself requires explanation. The primary assumption leaves us with one of two alternatives; either the extrasystoles are double from the first, or the alternation shown is *de novo* in its origin, that is to say, the heart has doubled its rhythm by a continuous interpolation of beats. The argument tends to weaken the primary assumption that extrasystolic and paroxysmal beats are of a like nature in so far as *this particular instance* is concerned.

† The borders of the areas damaged by the right and left coronary artery ligation are contiguous in the right ventricular musculature; if a specially excitable area is assumed, it necessitates the placing of the focus on this dividing line: the existence of a specially irritable focus upon this line is too improbable to render its assumption justifiable.

‡ By paroxysmal tachycardia proper is meant the periodic appearance of an accentuated rhythm arising suddenly and ending abruptly without the intervention of transitional rates.

ventricular musculature itself. In this type it may also be that from case to case the level of origin varies, but whether this is so or not, there is strong presumptive evidence in a given instance that such a rhythm is unifocal in origin. The absence of complete evidence, both in the case of the clinical "nodal or ventricular" paroxysms* and in the case of the experimental paroxysms described above, precludes their absolute identification one with the other at the present time. Neither is this identification essential. In both instances we are dealing with automatism of the musculature at a low level. In both we have, under consideration, a rhythm eminently pathological, in which the rate is far in excess of the normal sinus rate.† In both the sinus rhythm is dominated by the ectopic rhythm; in both the onset and offset are equally abrupt; in both a pronounced tendency towards termination in sudden death is manifested, in the experimental instance, and perhaps in the clinical instance also, the outcome of fibrillation. In both the ventricle exhibits signs of exhausted function, notably demonstrated by the co-existence of alternation in the force of the contractions, and by the dilatation of the heart. The analogy is close, and the underlying factors of causation have, therefore, much in common. And so, knowing that the experimental variety is a result of disordered nutrition, the outcome of anæmia, we are led to seek a similar pathogeny for the clinical variety. The human post mortem records are, at present, few, but in a case recorded by Mackenzie¹, it is reported that an artery supplying the bundle was obliterated.

The experimental evidence, by conclusively demonstrating the possible origin of a rapid ectopic rhythm in the ventricle, a division of the musculature known to possess under ordinary circumstances a grade of automatism which is comparatively low, arouses a conviction that under suitable circumstances a similarly accelerated rhythm may be generated at any level of the heart. Thus it happens that in those clinical paroxysms, where the auricle is pace-maker to the ventricle, but where otherwise the characteristics of the attacks are similar (the characteristics referred to are the sudden onset and offset, the accentuated rate and the variable pause which separates normal and ectopic rhythm), a like pathology is open to suspicion. And it further happens, when it is understood that the clinical evidence *per se* points to an

* One of the most striking evidences of the seat of origin of these rhythms is indirect. Clinically, they are so closely allied to nodal rhythm itself, that their entity with nodal rhythm is more than suspected. The electrocardiogram of nodal rhythm patients is almost constant from beat to beat and from case to case. The auricular wave is not to be found and the ventricular portion of the curve is often almost a duplicate of the normal ventricular curve. From this it may be argued that the contraction wave follows its usual course in the ventricle, or in other words, starts at or near the ventricular end of the A-V bundle. The similarity from beat to beat strongly supports the view that the rhythm is unifocal in origin. (This note is based upon an examination of 10 such patients and upon a comparison of the curves obtained with those published by Einthoven (*Archiv Internat. d. Physiol.*, 1906, iv, Fig. 31), and Hering (*Deutsch. Archiv f. klin. Med.*, 1908, xciv, Taf. II).)

† The rate of the nodal or ventricular paroxysm of man varies according to different observers from approximately 180 to 240 per minute.

intrinsic cardiac cause, that the proposition of a parallel causation enters the domain of rational hypothesis.

With a full consideration of the facts we are led to the anticipation that, just as extrasystolic contractions may spring from any level of the heart, and that such contractions are independent of the nervous supply, so likewise continuous rhythmic impulse formation at many levels will be found in the future. Neither can we draw any hard and fast line between the production of single impulses and successive impulses, in the present state of our knowledge. If, as evidence accumulates, it can be shown that the one is generated in some more primitive, or some specially modified portion of the musculature, the same evidence will support the origin of the other in similar tissue. It is to the primitive tissue, which Gaskell and others have shown to possess the property of rhythmicity in such marked degree, that the closest attention should be directed.

CONCLUSIONS.

1. Ligation of coronary arteries and their branches is a valuable method of investigating spontaneous extrasystoles (ectopic beats) and ectopic rhythms.

2. Ligation of the descending branch of the left coronary artery in dogs leads to ventricular extrasystoles, single, successive, and retrograde. They occur at varying intervals in diastole, and may give rise to bigeminy or trigeminy. Paroxysmal tachycardia is also produced.

3. Ligation of the complete right coronary vessel calls forth—auricular, “nodal” and ventricular extrasystoles, isolated at long intervals, frequent and regularly placed or in groups. Interpolations may occur. Paroxysmal tachycardia is also produced.

4. The paroxysmal tachycardia produced as a result of ligation of one or other artery is of very constant form, and occurs frequently. It consists of a rapid regular rhythm, having its origin in the ventricular musculature; it is not the result of altered innervation. Its rate varies from 140 to 420 per minute. It is usually paroxysmal, and the attacks last from a few seconds to 35 minutes.

5. The individual paroxysms are heralded by ventricular extrasystoles, many of which are retrograde. The irregularities disturbing the rhythm after its return to the normal are of a similar nature. It is probable that there is no essential difference between the impulses giving rise to extrasystolic and paroxysmal beat in most instances.

6. At the onset of a paroxysm the auricle may respond to sinus or ventricle, or may pass into fibrillation. Fibrillation of the auricle terminates in response to sinus or in response to ventricle.

7. The paroxysm of the ventricle terminates in a return to the normal rhythm, or more rarely in fibrillation of the ventricle; on two occasions it ended with the onset of a slow abnormal rhythm.

8. Reversed heart-block, showing most of the characteristics of the usual condition, is met with during the paroxysms.

9. Alternation is common during the paroxysms, and is not entirely dependent upon the rate with which contractions follow each other.

10. Paroxysmal tachycardia proper, as met with in experiment and in man, is the result of intrinsic change in the heart walls, giving rise to the production of ectopic impulses.

11. There is a gradual and not a sudden transition from the contractions of a rapidly contracting heart to those of fibrillation, the one condition passes insensibly into the other. The electrocardiogram of fibrillation is a very special one (Kahn), and appears to depend upon some general and comparatively slow underlying movement in the heart muscle.

12. In the interpretation of arterial pulse tracings, the relation of auricular to ventricular systole may be a very important one.

13. Retrogression of ventricular contraction to the auricle depends in some degree upon education of contraction in this direction. A systole of the auricle called forth in this way produces a highly atypical electrocardiographic curve. At present it cannot be concluded from the electric curves of nodal rhythm that the auricular contraction is absent.

14. Electrocardiographic curves afford valuable indications of the point of origin of those abnormal heart beats which are so frequently met with clinically.

15. In the dog the ventricle is certainly under control of the vagus, in some instances at least.

BIBLIOGRAPHY.

- 1. BAYLISS and STARLING. *Journ. of Physiol.*, 1892, XIII, 497.
- 2. KAHN. *Archiv f. d. ges. Physiol.*, 1909, CXXVI, 197.
- 3. KRAUS and NICOLAI. *Deutsche med. Wochenschr.*, 1908, I.
- 4. MACKENZIE. "Diseases of the Heart," London, 1908.
- 5. MILLER and MATTHEWS. *Archiv. of Internat. Med.*, 1909, III, 476.
- 6. PORTER. *Journ. of Physiol.*, 1894, XV, 121.
- 7. RIHL. *Zeitschr. f. exper. Path. u. Therap.*, 1905, I, 43.
- 8. TRENDLENBURG. *Archiv f. Anat. u. Physiol.*, 1903, Phys. Abth., 311.

ABBREVIATED PROTOCOLS.

Dog C.

- 12.23. First ligature applied, including the whole of the descending branch of the left coronary artery, and accompanying veins.
- 12.34. As no irregularity appears, a second ligature is placed at the termination of the same vessel.
- 12.42. The heart's action remaining regular, a third ligature is placed on the same vessel in the upper third of its course.
- 1.6. Both vagi divided. Heart still regular.
- 1.7. Occasional VEs*.
- 1.10. Frequent VEs.
- 1.12. Heart beating regularly. Fourth ligature placed to include the same artery, and a large branch springing from the lowest third of its course.
- 1.17. Frequent VEs, some early in the cardiac cycle and some late; occasional periods of bigeminy. Extrasystole in which A and V are premature and synchronous.
- 1.18. Frequent VEs.
- 1.20. Pulsus trigeminus (as a result of a single VEs occurring after each second normal beat).
- 1.24; 1.25; 1.30. VEs, usually single, occasionally two in succession; pulsus bigeminus. Extrasystoles in which the contraction in A† and V‡ is synchronous and premature; shortened pause.
- 1.35. Occasional VEs. Auricle beating regularly at 92; As-Vs = 0.10 sec..
- 1.40. Onset of paroxysm; V beating at 165 with marked alternation; A contracting at 90, complete dissociation; A responds very occasionally to V. The paroxysm lasts less than one minute, terminating in a ventricular pause of 0.75 sec.. The normal rhythm starts with response to A at 95; As-Vs§ = 0.11 sec.; VEs (single and in pairs) present.
- 1.43. Onset of second paroxysm; V rate 153; A responding with occasional dropped beat; Vs-As = 0.28 sec.. Paroxysm lasted about one minute.
- 1.44. Return to normal rhythm, with frequent VEs.
- 1.55-3.5. Heart regular; vagal stimulation slows whole heart with synchronous escape of A and V.
- 4.37. During the remainder of the experiment the heart beats regularly and normally, with the exception of a very occasional VEs, and extrasystoles, in which A and V contract prematurely and together. Numerous weak vagal stimulations invariably produce 2:1 heart-block during the continuation of the normal rhythm. The ventricle is faradised and fibrillates. The whole of the ligated area fails to fibrillate, it has been livid and ballooned during the greater part of the experiment.

* VEs signifies ventricular extrasystole.

† A = auricle.

‡ V = ventricle.

§ As = auricular systole; Vs = ventricular systole. As-Vs = interval between onset of auricular and ventricular systole.

Dog G.

- 11.49. Ligation of the whole right coronary artery.
- 11.52. First irregularity noted.
- 11.53. AEs* single and successive.
- 11.57. Both vagi cut.
- 12.0. Right ventricle not contracting perceptibly. Heart regular. Stimulation of vagus causes slowing of the whole heart with escape of A.
- 12.10. Vagal stimulation causes slowing of whole heart with staircase in force of auricular contraction on recovery, on two occasions.
- 12.47. Heart beating regularly since 12.10, with very occasional VEs.
- 1.12. Normal rhythm with occasional VEs; rate 105; As-Vs = 0.12 sec..
- 1.14. Onset of paroxysm. Rate of V 170 regular; A responding regularly. Vs-As = 0.13 sec. (As-Vs = about 0.23 sec.).
- 1.15. Irregular bigeminal action of V; A responding to each beat. Rate 180; Vs-As constant at 0.14 sec.; As-Vs varying from 0.2 to 0.5 sec..
- 1.16. Stimulation of vagus produces dropping out of 3 auricular beats in 4. V unaffected.
- 1.20. Vagal stimulation produces 2:1 reversed heart-block. Later AEs occurs with full pause.
- 1.25. Same rhythm continues. Rate 210. Vs-As = 0.15 sec..
- 1.26. Auricular response occasionally missed. Rate 180.
- 1.28. Same rhythm. A and V beating at 228. Vs-As = 0.16 sec..
- 1.45. Same rhythm has continued until this time, when V fibrillates.

Dog H.

- 12.23. Ligation of right coronary vessels. Immediately followed by lividity of the whole muscle included.
- 12.36. Both vagi cut. Rate 72; As Vs = 0.12 sec..
- 12.41. Stimulation of vagus causes slowing of the whole heart with staircase in the force of auricular contraction on recovery.
- 12.45. First irregularity observed. Not recorded.
- 12.52. Frequent single extrasystoles. A and V both premature. Pause almost full. Vs-As of extrasystole = 0.13 sec..
- 12.58. Occasional AEs with shortened pause.
- 12.59. AEs and REs†.
- 1.6. Frequent Es of several types. AEs, early and late; REs, early and late, and in groups.
- 1.12. Occasional AEs.

* AEs = auricular extrasystole.

† REs is used to designate the extrasystoles described at 12.52 of this experiment; they are those in which A and V are premature and in which the Vs-As interval is of such a length that As may be considered as a response to Vs.

- 1.14. Groups of successive AEs.
- 1.15; 1.17. Frequent Es of the forms above described. Bigeminus as a result of AEs.
- 1.20. AEs and extra beats in which A and V contracted prematurely and synchronously.
- 1.58. Same irregularities continue, mixed with VEs. Rate 48. As-Vs = 0.12 sec..
- 2.0. Onset of paroxysm. V at 375; A fibrillating. Later, V at 180, with marked alternation; A still fibrillating. Later still, A and V beating at 183; Vs-As = 0.13 sec..
- 2.1. Same continues. Vagal stimulation produces 4:1 heart block, V unaffected. Later, stimulation produces falling out of 5, 3, and 7 A beats.
- 2.2; 2.3; 2.5; 2.7; 2.9. Same rhythm continues. Vagal stimulation produces falling out of 4 and 10 A beats. Vagal stimulation yields 4:1 reversed heart-block.
- 2.28. Rate has now dropped to 140. Vs-As interval 0.15 sec. Weaker vagal stimulation gives 2:1 reversed heart-block, and decreases auricular excursion.
- 2.30. Vagus stimulation (stronger) stops A for 15 beats; V unaffected.
- 2.34. Same continues. Rate of V 206; A at 103.
- 2.35. During the next minute the ventricular excursion gradually decreases. The curves pass insensibly into those of fibrillation. With the establishment of ventricular fibrillation the auricle recommences to respond to the sinus.

Dog I.

- 1.15. Ligation of right coronary vessels. Followed by alternation of auricle, with gradual recovery from the same.
- 1.17. Ventricular muscle dark and bulged. A and V show a synchronous alternation.
- 1.25. The same. Rate 150. As-Vs = 0.08 sec..
- 1.30. Both vagi divided. Vagus stimulation causes slowing of whole heart, followed by staircase in force of auricular contractions on three occasions. Vagus stimulation causes slowing of whole heart with separate escape of A and V, followed by staircase in force of auricular contractions.
- 1.47-2.6. Occasional AEs and VEs.
- 2.9. Frequent VEs.
- 2.15. Bigeminy due to VEs; occasional AEs and pairs of VEs.
- 2.20. Frequent VEs and REs. Rate 152; As-Vs = 0.11 sec..
- 2.25. Paroxysm begins. V at 224; A at 156, but irregular (probably occasional responses).
- 2.28. Same continues; V at 312 (later 289); A at 156, but still irregular. V beats show occasional bigeminy.
- 2.30. Same continues. Vagal stimulation has little effect on either A or V, on two occasions. Rate of A and V, 203. Stronger stimulation stops A and V. Ventricular pause 1.2 sec., Auricular 1.1; return to normal rhythm for two cycles.
- 2.33. Paroxysm continues; V at 300, alternation marked. A fast and very irregular. Rate about 300.
- 2.36. Same continues. V at 272; A at 136; Vs-As = 0.11 sec.. Two AEs occur without interruption of ventricular rhythm.
- 2.40. V fibrillating; A beating at 76.
- 2.45. A continues to beat slowly and irregularly.

Dog J.

- 1.15. Ligation of right coronary vessels. Rate 162; As-Vs = 0.09 sec..
- 1.17. Left vagus divided. Stimulation causes slowing of whole heart with single dropped beat of V.
- 1.30. Numerous and successive VEs. Occasional REs. Rate 160; As-Vs = 0.09 sec.. Later, onset of paroxysm. A and V at 192. Vs-As = 0.15 sec.. Vagal stimulation produces 5 dropped auricular beats, followed by reversed heart-block, 2:1. Vagal stimulation gives marked auricular slowing. A little later V pauses 1.1 sec., and there is a return to the normal rhythm for a few beats. The paroxysm starts again. Vagal stimulation produces reversed heart-block. Vagal stimulation produces marked slowing of A. In each case V unaffected.
- 1.36. Right vagus cut. Paroxysm continues. V at 234; A at 156. Complete dissociation. Later, A and V at 193. Vs-As = 0.14 sec.. Venous curve shows two waves falling during ventricular systole.
- 1.55. Same continues. A and V at 142; Vs-As = 0.13 sec..
- 1.59. Same continues. V at 270; A at 135; Vs-As = 0.13 sec..
- 1.59½. A faradised, fibrillation. V continues to beat at 225.
- 2.0. V fibrillating.

Dog K.

- 12.7. Ligation of right coronary vessels. Rate 108; As-Vs = 0.11 sec.. Commencing lividity of the ventricular musculature involved is immediate.
- 12.10. First irregularity; not recorded.
- 12.16. Both vagi divided. Rate 97.
- 12.30. VEs are occasional.
- 12.45. VEs are numerous, single and grouped.
- 12.50. AEs and VEs.
- 12.51. Interpolated VEs. Rate 92. Accompanied by prolonged Vs-As interval.
- 12.52. The same irregularity. Also successive VEs.
- 12.54. Bigeminy of V, resulting from VEs following each rhythmic beat.
- 1.4. Numerous VEs, some interpolated, many in groups.
- 1.10. The same continues. Rate 91; As-Vs = 0.09 sec..
- 1.20. Onset of first paroxysm. Rate of V 206; A 103; Vs-As = 0.14 sec..
- 1.21. Normal rhythm.
- 1.35. Normal rhythm. Rate 87; As-Vs = 0.11 sec.; VEs.
- 1.35. Onset of second paroxysm. Rate of A and V, 157.
- 1.36. Same continues. Rate of V 234; of A 117; Vs-As = 0.15 sec..
- 1.37. Normal rhythm with REs (very numerous).

- 1.47. Same continues. Rate of heart 70; As-Vs = 0.10 sec..
- 1.48. Onset of third paroxysm. Rate of V 192. Occasional failure of response by A; Vs-As variable. Vagal stimulation causes pause of V for 1.5 sec., and of A 1.3 sec., with return to the normal rhythm, with REs. Rate 96; As-Vs = 0.12 sec..
- 1.49. Directly afterwards the paroxysm starts again. Rate of A and V 157; Vs-As = about 0.12 (variable and longer at first) (Fig. 2).
- 1.50. Vagal stimulation leads to return to the normal rhythm, interrupted by numerous REs. The interval Vs-As of these beats varies from 0.12 to 0.18 sec..
- 1.52. Bigeminy of A and V due to REs (Fig. 13).
- 1.55. The same rhythm continues, interrupted by many VEs, most of which disturb the auricular rhythm (REs).
- 2.10. Similar events continue. VEs and REs very numerous.
- 3.20. Same has continued until at this time V and A enter the fibrillary state.

Dog M.

- 12.1. Ligation of right coronary vessels. Rate 172; As-Vs = 0.08 sec..
- 12.20. Both vagi divided.
- 12.25. Muscle has been ballooned for some time.
- 12.40. Vagus stimulation stops the whole heart for 3 sec..
- 12.45. First irregularity. Bigeminy as a result of VEs.
- 12.52. VEs and REs are numerous. The Vs-As interval of the latter is 0.15 sec..
- 12.58; 1.4. Successive VEs and occasional REs.
- 1.15. The same continues; pairs of VEs are present of which the second beats are retrograde (Fig. 1).
- 1.29. Bigeminy due to VEs; occasional REs.
- 2.0; 2.5. AEs, VEs, and REs are present in large numbers.
- 2.6. VEs and REs. Rate 149; As-Vs = 0.10 sec..
- 2.7. Onset of first paroxysm. Rate of V 220; of A 110; Vs-As = 0.12 sec.. Later, the rate quickens, and the ratio of $\frac{V}{A} = \frac{3}{2}$ (Fig. 7).
- 2.9. Vagus stimulation causes return to normal rhythm.
- 2.17. Rate 91; As-Vs = 0.10 sec.. Frequent VEs present.
- 2.20. Onset of second paroxysm. Rate of V and A 174; Vs-As = 0.14 sec.. Later, A misses an occasional beat.
- 2.23. Vagus stimulation causes dropping out of A, with prolongation of Vs-As (Fig. 9).
- 2.24. Normal rhythm, regular. Rate 94; As-Vs = 0.10 sec..
- 2.35. VEs and REs disturb normal rhythm. Rate 107; As-Vs = 0.11 sec..
- 2.36. Onset of third paroxysm. Rate of V and A 156; Vs-As = 0.14 sec.. An AE has full pause, and does not affect V. Stimulation of vagus results in a return to the normal rhythm, interrupted by REs (Fig. 10).

- 2.37. Normal rhythm, frequent VEs.
- 3.0. Normal rhythm, occasional VEs.
- 3.10. Experiment stopped.

Dog O.

- 12.13. Ligation of right coronary vessels. Rate 165.
- 12.15. Both vagi divided. Stimulation of vagus causes marked slowing of the whole heart.
- 12.24. First irregularity.
- 12.25; 12.26; 12.28; 12.29; 12.30; 12.35; 12.36. Numerous and successive VEs.
- 12.36. Rate 168; As-Vs = 0.08 sec.. Numerous and successive VEs.
- 12.40. Onset of first paroxysm. V at 356; A at 165. Alternation extreme (Fig. 4). At first dissociation; later, A fibrillates.
- 12.40½. Rate of V 345; marked alternation.
- 12.41. Rate of V 340; marked alternation, small beats coming through to carotid.
- 12.42. V rate gradually drops from 310 (Fig. 8) to 290; rhythm of A as 1:4. Alternation absent.
- 12.42½. Onset of slow rhythm, chiefly retrograde. Rate 73. Venous pulse shows two waves falling in Vs. The rhythm passes gradually into a mixed response of A to V and sinus. Rate about 48. Later, an irregular rhythm with response of V to A, and an occasional REs.
- 12.44. Regular normal rhythm; rate 128.
- 12.46. VEs single and successive; bigeminy of V.
- 12.50. Regular normal rhythm. Rate 158; As-Vs = 0.07 sec..
- 12.51. Onset of second paroxysm. V at 374; A at 160. Complete dissociation. Later, A fibrillates, and on recovery responds to alternate V contractions. V at 380; alternation extreme (Fig. 5). Vagal stimulation produces dropped A beats. Later V at 380; A at 150 responding with dropped beats. Alternation marked, weaker beats now appear in carotid curve. Vagal stimulation converts a 3:2 to 4:1 heart-block.
- 12.53. Spontaneous offset of paroxysm to a slow mixed rhythm, chiefly retrograde. Rate about 74.5 (Fig. 12).
- 12.54. Onset of third paroxysm. V at 294; A at 147.
- 12.55. Vagal stimulation causes falling out of A beats.
- 12.58. Rate of V rises to 397 and 405; A fibrillating; carotid monoelectric (Fig. 6).
- 1.0. V follows A into fibrillation.

Dog P.

- 12.25. Ligation of right coronary vessels. Rate 185; As-Vs = 0.08 sec..
- 12.36. Vagus stimulation, whole heart stops for about 3 sec., staircase of A in recovery, on three occasions.
- 12.45. First irregularity occurs. Both vagi divided. VEs. Rate 108; As-Vs = 0.08 sec..

- 12.57. Onset of first paroxysm. V at 260; A fibrillating. Later, return to normal sequence. Rate 172; As-Vs = 0.08 sec..
- 12.59. Normal rhythm. Rate 180; As-Vs = 0.08 sec..
- 1.0. Onset of second paroxysm. V at 257. From tracing of A it is impossible to interpret events. The curve gives the impression of being a transition between contraction and fibrillation.
- 1.1. Normal rhythm.
- 1.15. Normal sequence. Rate 168; As-Vs = 0.08 sec..
- 1.28. Onset of third paroxysm. Rate of V 202; A in same state as in second paroxysm. Later, return to normal rhythm.
- 1.30. VEs.
- 1.38. Frequent VEs. Rate 164; As-Vs = 0.09 sec..
- 1.40. Onset of fourth paroxysm. Rate of V 271; A at 164; independent. Later, return to normal rhythm. Rate 168; As-Vs = 0.10 sec. (Fig. 3). Later, normal rhythm with VEs. Later, a fifth paroxysm. Rate of V 238; of A 161; independent; lasting a few seconds. Return to normal rhythm at 161, with successive VEs; As-Vs = 0.08 sec..
- 1.41. Onset of sixth paroxysm. V at 206; A at 165; independent.
- 1.48. Termination in normal rhythm; single beat only. Note constancy of A rates. Later, onset of seventh paroxysm. V at approximately 235; A fibrillating. Later, change to normal rhythm at 152; As-Vs = 0.10 sec..
- 1.49-1.52. Normal sequence. Rate 160. Numerous VEs; occasional REs.
- 1.55. Numerous and successive VEs. Rate 157; As-Vs = 0.10 sec. (Fig. 11).
- 1.56. Onset of eighth paroxysm. V at 348; A at 174; Vs-As = 0.11 sec.. Alternation extreme. Gradual development of alternate beats, as V rate falls to 280, and A responds 1:2; Vs-As = 0.12 sec.. Rate of V rises to 320, and falls to 264. A still responding to alternate beats; Vs-As = 0.10 sec.. Vagus stimulation causes appearance of 4:1 reversed rhythm. Later, it produces dropping out of A beats on three occasions.
- 1.59. Vagus stimulation causes dropping out of A beats.
- 2.0. Rate of V 251; A beating at 152. Rhythm independent.
- 2.6. V beating at 225; A fibrillating.
- 2.10. V fibrillates.

Dog R. Electrometer curve replaces carotid curve.

- 11.45. Ligation of right coronary vessels.
- 12.0. Regular rhythm. Rate 175; As-Vs = 0.09 sec.. P and R well-marked; T inverted. P starts 0.04 sec. before onset of As. R starts 0.04 sec. before onset of Vs. P-R = therefore 0.09 sec..
- 12.5. First irregularities. Single and successive VEs. The ventricular extrasystole is composed of two peaks; P falls before, after, or upon one or other peak. Rate 172.
- 12.7. Very frequent VEs. Groups of three are common.
- 12.10. The same continues. The last extrasystole of a group is often retrograde.

12.17. The same (Fig. 14).

12.20-12.55. The same (Fig. 15). Rate has dropped to 142.

12.56. Onset of paroxysm. Rate of V = 420; A at about 70, but varying (Fig. 16). The ventricular curve shows alternation, the electrometer curve shows it only occasionally, and it is then expressed by an alternate deepening of the dips between the beats. The curves pass directly into ones in which both ventricular and auricular tracings show small undulations, which are at times regularly placed, and in which the electrometer curve shows a succession of peaks, two of which correspond to each undulation of the V tracing; these peaks are, as a rule, irregularly placed, but at times are regular; the rate, reckoning two peaks as a beat, is at about 420. The undulations on the V curve spread out more and more, and the peaks on the electrometer curve correspond. Visible fibrillation of V is starting. The electrocardiographic curve passes gradually into the wide and irregular undulations recorded by Kahn (rate about 180); A is no longer beating; the V tracing shows undulations exactly corresponding to the galvanometer curves. The paroxysm proper lasted less than 1 minute.

THE ACTION OF AN ACTIVE PRINCIPLE FROM APOCYNUM.

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I. HISTORICAL AND INTRODUCTORY.

APOCYNUM has for many years enjoyed a somewhat varying reputation in therapeutics, chiefly as an alternative to digitalis. The earlier clinical observers (Knapp, Griscom¹²) who appear to have tried the drug on the strength of its reputation among the American Indians, describe it as emetic, cathartic, diaphoretic, and diuretic. Later clinical observers, such as Dabney¹, laid special emphasis on its diuretic action. Dabney's paper contains a number of references to similar clinical observations. Husemann¹³ appears to have first pointed out that this drug, like other members of the Apocynaceæ (Oleander, Strophanthus), contained a heart-poison belonging to the Digitalis group. Bradford is reported by Murray¹⁰ to have found that it resembled Strophanthus in its action on the heart, but that its powerful effect on the vagus mechanism, and the absence of a vaso-constrictor effect, prevented it from producing any rise of blood pressure. In 1883 Schmiedeberg²² separated from it two indefinite products which he termed Apocynin and Apocynëin. Apocynin was an amorphous non-glucosidal body, almost insoluble in water, readily soluble in alcohol and ether, which caused systolic arrest of the frog's heart in very small doses. Apocynëin was an amorphous glucoside resembling digitalein.

In 1888 Sokoloff²³ examined the action of Apocynum on mammals. He found that an extract (he used an 8 per cent. watery infusion of the rhizome), when injected intravenously in doses of from 3 to 10 cc., caused, in the first place, a pronounced retardation of the heart's action, the pulse wave being enlarged, and the blood pressure raised: later, the initial retardation gave way to a secondary acceleration of the heart, the arterial pressure rising still further. He stated that the initial slowing of the heart was caused by a stimulation of the cardio-inhibitory centre, and of the peripheral inhibitory mechanism. The subsequent acceleration was not due to actual paralysis of the inhibitory apparatus, since injection of another dose of the drug could again produce retardation. Large doses produced a third stage of arrhythmia

* The experiments at Guy's Hospital were performed by P. P. Laidlaw only.

of the heart, with undulating blood pressure, which ultimately fell to zero with failure of the heart. Sokoloff attributed the rise of blood pressure, during the first and second stages of the action, to stimulation of the vaso-motor centre in the medulla, of the spinal vaso-motor centres, and also, to some extent, of the heart and blood-vessels themselves.

In 1904 H. C. Wood, Jr.²⁶, reinvestigated the drug physiologically and chemically. His physiological results were in the main similar to those of Sokoloff. Wood, however, concluded that the constriction of the arterioles was mainly, if not entirely, due to direct stimulation of their muscular walls. He also stated that the vagus became refractory to stimulation during the second stage of cardiac acceleration, and pointed out the characteristic death by sudden heart-failure caused by large doses of the drug. Chemically he advanced but little beyond Schmiedeberg's results: but he made the significant observation, that a crystalline substance, obtained commercially as Apocynin, was practically inert, and that the corresponding crystalline substance which he prepared himself, though very active when first isolated, gradually lost activity with successive purifications. He conjectured, rightly as now appears, that the activity was due to some very highly active impurity adhering to the crystalline Apocynin. Because the activity of the mother liquors and extracts was destroyed by boiling with dilute acids he supposed that the active substance was glucosidal in nature, but he did not succeed in separating it. In 1908 H. Finnmøre²⁷ described his identification and synthesis of the crystalline Apocynin, which proved to be Acetovanillone. One of us (P.P.L.) found that this synthetic Apocynin had only a very slight activity, thus confirming Wood's suggestion with regard to the pure Apocynin.

Early in the present year Finnmøre²⁸ published a preliminary note on the isolation, from *Apocynum cannabinum*, of a crystalline bitter principle, which he called "Cynotoxin," and which one of us (P.P.L.) had found to possess, in a very intense degree, the characteristic action of Apocynum. Finnmøre believes that it is "a dilactone, either of Kiliani's digitic acid or of a closely related isomeride." C. W. Moore²⁹ published almost simultaneously the results of an independent and very exhaustive investigation of the constituents of *Apocynum androsaemifolium*, from which he had also isolated the bitter principle, to which the name "Apocynamarin" was assigned. This substance had also been ascertained by one of us (H.H.D.) to be the essential active principle. Moore considers it possible that Apocynamarin is the "dilactone of Kiliani's oxy-digitogenic acid, or of an isomeride."

A comparison of our results, when we discovered the duplication, showed us that the principles thus separately isolated were identical in physiological action, and we have thenceforth conducted the investigation together. Unfortunately, it is impossible, at present, to assume the chemical identity of the bitter principles from the two species. Though they agree in physical properties, the formulæ assigned to them by their respective discoverers are not the same. Cynotoxin, according to Finnmøre's preliminary

note, has the formula $C_{25}H_{38}O_6$. Apocynamarin, according to Moore, has the formula $C_{25}H_{36}O_6 \cdot 2H_2O$.* In our further physiological investigation of the two preparations we were unable to detect any qualitative or quantitative difference between them, and ultimately used one or the other indifferently. While the question of chemical identity remains open, we have no choice but to use, in describing any experiment, the name indicating which preparation was actually employed. But it must be understood that whenever we attribute an action to Cynotoxin an identical effect, in sign and degree, is obtainable with Apocynamarin, and *vice versa*. It may be noted incidentally that the identity of action disposes of the statement, which has obtained currency in the literature of the subject, to the effect that *Apocynum androsamifolium*, which is often used instead of *Apocynum cannabinum*, is devoid of the specific activity of the latter†.

II. THE ACTION OF APOCYNIN (ACETOVANILLONE).

The experiments have been made with synthetic and natural preparations made by Finemore, and a specimen of the natural substance obtained by Moore from *Apocynum androsamifolium*. These were not perceptibly different in action.

The only definite effects which we have been able to detect as a result of the administration of Apocynin were upon the vascular system. When 10 mg. of Apocynin are injected into an intact frog the only effect to be noticed is that the frog remains quiet and motionless for a time and then recovers. Reflexes persist throughout. If the dose is injected into the dorsal lymph sac of a pithed frog, with the heart exposed, there is observable a gradual slowing of the heart-beat without much increase in strength; both systole and diastole are prolonged, but the latter more conspicuously. Larger doses (up to 25 mg.) cause a still further slowing of the heart by prolongation of the diastole, and the beat becomes weaker. In no case does Apocynin cause systolic arrest of the heart. The effects produced by direct application of the drug, in 1 per cent. solution, to the exposed heart are similar to those resulting from injection. Fig. 1 shows the effect on the frog's heart.

The isolated mammalian heart, perfused with oxygenated Ringer's solution by Locke's method, shows similar results, viz., a slight increase in amplitude of beat with very slight slowing. Large doses produce a more marked slowing with considerable diminution in force (see Fig. 2).

Injected intravenously into anæsthetised animals (cats, dogs, and rabbits were used), Apocynin was found to cause a slight, transient rise of

* It appears that the difference between the formulae really depends for the most part on the water of crystallisation (cp. Moore, loc. cit.).

† The United States Pharmacopœia, under the title "Apocynum," recognises "The dried rhizome of *Apocynum cannabinum*, or of closely allied species of *Apocynum*."

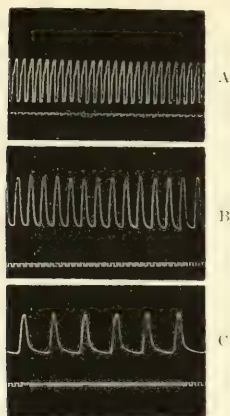


Fig. 1. $\times \frac{2}{3}$ linear. Frog's heart, suspension method. Upstroke = systole. A—Normal. B—30 sec. after intravenous injection of min. viii of 0.5 per cent. Apocynin in Ringer's solution. C—After further injection of min. v of the same solution.

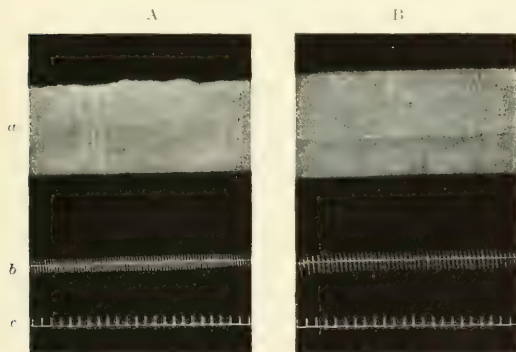


Fig. 2. $\times \frac{2}{3}$ linear. Isolated rabbit's heart, perfused with Locke-Ringer solution. A—Perfusion with plain Locke-Ringer. B—One minute after substitution of 1:15,000 Apocynin. a—Ventricular beat; b—Drop-record of coronary outflow; c—Time in seconds.

blood pressure. A small acceleration of urinary flow was noticed in one experiment.

It is somewhat unfortunate that the name Apocynin has been applied to several different substances. It is clear that the crystalline substance, known commercially as Apocynin, and identified by Finnemore as Acetovanillone, plays practically no part in the specific action of the drug. Schmiedeberg's "Apocynin," on the other hand, appears to have been physiologically potent, but was evidently a mixture of substances, among which were probably both acetovanillone and the true active principle described in the next section. The resinous products called "Apocynin" by early observers, such as Griscom, were chemically even more indefinite. The fact, first demonstrated by Wood, that the natural crystalline Apocynin is purified only with some difficulty from traces of the true active principle, might be regarded as accounting even for the small degree of activity which we detected. Such a supposition, however, is excluded by the identical activity of synthetic acetovanillone.

In addition to free Apocynin (Acetovanillone) Moore isolated from *Apocynum androsaemifolium* a glucoside of that substance to which he gave the name "Androsin." This, however, we found to be even less active than the Apocynin itself. The observation has, therefore, no connection with Wood's suggestion that the active principle is a glucoside which loses its activity on hydrolysis. The true explanation of Wood's experience is given in the next section.

III. THE BITTER PRINCIPLE [CYNOTOXIN (FINNEMORE), APOCYNAMARIN (MOORE)].

It will be clear from the descriptions, reproduced above, by various observers of the action of extracts of Apocynum, that the essential active principle must possess in a high degree an action of the general type known as a "digitalis" action. It will be shown that this is true of the bitter principle isolated independently by Finnemore¹⁰ and by Moore¹¹ from the two species. It is a neutral crystalline principle, with an intensely bitter taste, and is only slightly soluble in water or physiological saline solution at the ordinary temperatures, though its solubility increases rapidly with rise of temperature. It is not a glucoside, though boiling with acids or alkalis destroys its activity; this fact forms the basis of Wood's suggestion as to the glucosidal nature of the active principle. Solutions for experiment were made by dissolving 20 mg. of the substance in 0.5 cc. of absolute alcohol; this was mixed with 40 cc. of hot physiological saline. Such a solution (1:2,000) was stable on cooling to room temperature. With higher concentrations crystallisation always took place after a time.

As stated above, the action belongs to the digitalis type. We have experimented on the frog and on mammals.

A. EXPERIMENTS ON THE FROG.

An intact frog when a lethal dose of the principle (about 0.2 mg. per 100 gm.) is injected into the dorsal lymph sac, shows no symptoms for some time after the injection. At from 1 to 1½ hours after the injection it becomes less active, squats on the table with its head touching either the fore-limbs or the table itself. When disturbed it moves slightly and assumes a normal attitude only to sink back in the course of a minute or so to its former position. A little later it will no longer recover when placed upon its back, and respiration fails. Within three hours reflexes disappear. Post mortem the ventricle is found to be in systole, the auricles engorged with blood. The minimal lethal dose per 100 gm. of frog is about 0.2 mg.

DETERMINATION OF LETHAL DOSE OF APOCYNAMARIN FOR THE FROG.
(R. TEMPORARIA).

| WEIGHT. | DOSE. | DOSE PER 100 gm. | RESULT. |
|---------|----------|------------------|-------------------|
| 26 gm. | .066 mg. | .25 mg. | † 1st hour |
| 26 .. | .066 .. | .25 .. | † 1st hour & half |
| 24 .. | .05 .. | .21 .. | † 1st hour |
| 24 .. | .05 .. | .21 .. | † 2nd hour |
| 27 .. | .06 .. | .22 .. | † 2nd hour |
| 30 .. | .06 .. | .2 .. | † 2nd hour |
| 30 .. | .06 .. | .2 .. | † 2nd hour |
| 30 .. | .06 .. | .2 .. | * lived |
| 30 .. | .057 .. | .19 .. | lived |
| 30 .. | .055 .. | .18 .. | † 2nd hour |
| 30 .. | .055 .. | .18 .. | lived |
| 30 .. | .055 .. | .18 .. | lived |
| 26 .. | .047 .. | .17 .. | lived |
| 26 .. | .047 .. | .17 .. | lived |
| 25 .. | .047 .. | .17 .. | lived |

Strophanthin (from *Strophanthus gratus*) has an M.L.D. of between .07-.08 mg. per 100 gm. frog.

Apocynamarin or *CYNOTONIN* has, therefore, about $\frac{1}{2}$ - $\frac{1}{3}$ of the activity of Strophanthin on the frog's heart.

* died next morning.

Its action on the frog's heart is readily demonstrated by pithing a frog, injecting a few drops of 1 in 2,000 solution in physiological saline into the dorsal lymph sac, and exposing the heart. The suspension method will give a graphic record of the results. The first effect is to increase the contraction of the ventricle, systole being more complete. As the substance continues to be absorbed the ventricle is gradually thrown into complete systole. There are noticeable areas of systole, usually more marked at the apex, which persist during diastole of the remainder. These systolic areas increase in size until they involve the whole ventricle. Congestion of the auricle and great veins becomes very marked towards the end, as the output of the ventricle diminishes. Just before the final stage of complete systole one receives the impression that the auricle by its systole is distending a tonically contracted ventricle, and the ventricular contraction, when it develops, is like a slow peristaltic wave. The auricle continues to beat for a

short time after the ventricle remains firmly contracted. Fig. 3 shows the result of recording by the suspension method at various stages.

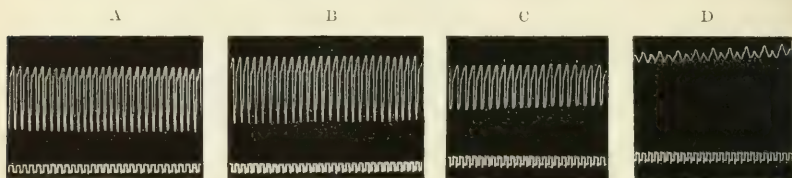


Fig. 3. Heart of decerebrate frog. Suspension method. Upstroke = systole. Min. vii 1:5,000 Cynotoxin injected into dorsal lymph sac. A—Normal. B—3 minutes after injection. C—6 minutes after injection. D—10 minutes after injection. Time in seconds.

Tracings of isolated frogs' hearts, perfused with Ringer's solution (through the sinus venosus), were also taken; addition of Cynotoxin caused the development of a precisely similar series of phenomena, to those observed in the pithed amphibian. To obtain a measure of the ventricular volume under the influence of the drug, we used Locke's modification of Williams' apparatus*. This gives an accurate record of the output of the ventricle while the heart perfuses itself. We found Dixon's⁶ frog-intestine volume-recorder very useful with this apparatus. Cynotoxin or Apocynamarin in quite weak concentration (1 in 500,000 to 1 in 200,000) produces an increased output, and a very similar sequence of effects to those observed in pithed animals, concluding with systolic arrest (Fig. 4). One variation should be mentioned; the initial decrease of volume frequently gives way to a secondary dilatation, the tonus subsequently recovering, and then increasing till systolic arrest becomes complete. This difference is doubtless due to the fact that, in the perfusion apparatus, the pressure on the interior of the ventricle remains constant, and may secondarily distend the ventricle in spite of its systolic effort. Indeed, with a sufficiently high inflow pressure, a final quiescence in a condition of distension, simulating true diastole, may be obtained. In the pithed frog, on the other hand, the pressure falls with the failing output, and nothing but the efforts of the auricle hinders the passage of the ventricle into complete contraction.

In addition to this characteristic digitalis-like action on the frog's heart Cynotoxin or Apocynamarin has a pronounced effect on the plain muscular tissues of that animal. The action was examined on:—

1. The plain muscle of the arteries;
2. The plain muscle of the stomach.

* This apparatus was shown at a meeting of the physiological society, but a full description has not yet been published. Through the kindness of Dr. Locke we have been able to use it in the incomplete form.

For recording the former a fine cannula was inserted into the aorta, and the vessels washed out with Ringer's solution. The sinus was laid open freely. The frog was placed in a funnel and its vessels perfused with Ringer's

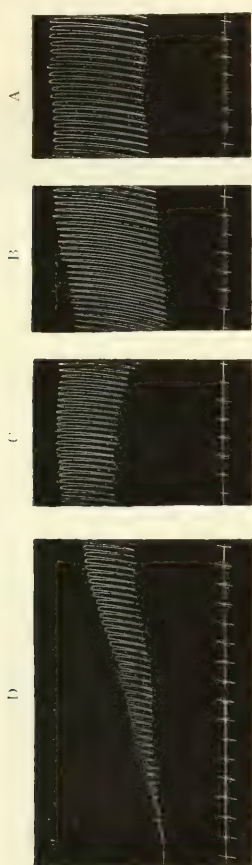


Fig. 4. $\times 11$ linear. Frog's heart (Loe-Le Williams apparatus, Dusen volume recorder). Perfusion with Ringer's solution, changing to 1:100,000 Apocynum in Ringer. Downstroke—systole. A—Normal. B—Just after Apocynum reaches the heart. C—Later (secondary dilatation). D—Passing into permanent systole.

solution under constant pressure. The rate of outflow from the funnel was recorded with a drop-counter or by collecting in a graduated cylinder. The injection of Apocynamarin or Cynotoxin into the perfusion cannula caused a

pronounced diminution of venous outflow. Fig. 5 shows the result of a comparison between 1 mg. of Strophanthin (known to be a very active specimen) and $\frac{1}{3}$ mg. Cynotoxin. It will be seen that the Strophanthin caused a very slight slowing, while Cynotoxin diminished the venous outflow by about one-half. It is, therefore, a much more powerful vaso-constrictor than Strophanthin. The dose given was, of course, large.



Fig. 5. $\times \frac{1}{2}$ linear. Perfusion of frog's blood-vessels at pressure of 30 cm. Ringer's solution. Drop record of outflow, drops averaging 6 to 1 cc. At A—1 mg. Strophanthin injected into perfusion cannula. B— $\frac{1}{3}$ mg. Cynotoxin.

The frog's stomach showed a similar response. The technique employed was that described by Dixon⁷ when studying the innervation of this organ. A frog's stomach, carefully filled with Ringer's solution, was connected with a U tube and a slight positive pressure maintained. The other limb of the U tube was connected to a Dixon volume-recorder. When 1:5,000 Apocynamarin was applied to the outside of the stomach the rhythmic movements were replaced by a prolonged intense contraction (Fig. 6). It should be noted that larger doses are required to induce good responses in plain muscle than those which suffice to produce a pronounced effect on cardiac muscle.

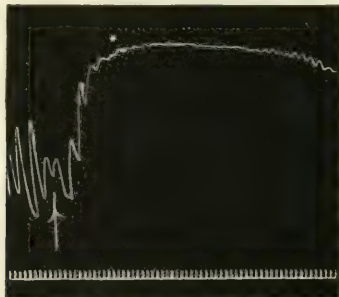


Fig. 6. $\times \frac{1}{2}$ linear. Volume-record of frog's stomach. Distension-pressure = 18 cm. of water. Upstroke = contraction. At $\frac{1}{2}$ 1:5,000 Apocynamarin in saline solution applied to the exterior.

On skeletal muscle Apocynamarin or Cynotoxin has no effect in small doses. A muscle-nerve preparation from a frog killed with Apocynamarin will respond normally when stimulated through the nerve or directly. Reflexes in the spinal frog are still obtainable for some time after the heart is systolised. But, like other members of the digitalis series, Apocynamarin presents a curare-like action if a muscle-nerve preparation is immersed in a solution of the substance of sufficient concentration. A nerve-muscle preparation was soaked for half an hour in physiological saline solution, 0.6 per cent., containing a little alcohol ($\frac{1}{2}$ cc. in 20 cc.), and sufficient Apocynamarin to give a concentration of 1 in 2,000. At the end of this time the muscle would no longer respond to any stimulus applied to the nerve, but it was almost normally responsive to direct stimuli. Control muscles, soaked in physiological saline with the same proportion of alcohol only, responded normally to both direct and indirect stimulation. The curve obtained by direct stimulation of the poisoned muscle was slightly flatter than that given by the control, and showed a trivial prolongation of the relaxation period.

NOTE ON THE ACTION ON THE TOAD'S HEART.

It has been known for many years that the heart of the toad is relatively very resistant to the poison which the animal's skin secretes (Vulpian²²), and which is present in a recognisable amount in its blood (Phisalix and Bertrand²³). In its action on other animals this toad poison, "Bufotalin" (Faust⁴), resembles the members of the digitalis series, and it was observed

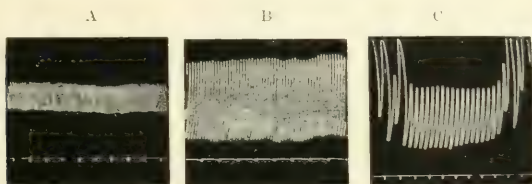


Fig. 7. $\times \frac{1}{2}$ linear. Toad's heart (Locke-Williams apparatus; Dixon recorder). Perfusion with a mixture of blood and Ringer's solution. The heart had already been perfused with 1 : 22,000 Apocynamarin, and in 1 : 5,000 Strophanthin. A—After return to plain blood—Ringer. B—After 2 hours perfusion with 1 : 50,000 Apocynamarin in blood—Ringer. C—After 16 hours continuous perfusion with 1 : 50,000 Apocynamarin.

that the toad's heart is similarly resistant to other members of that series (Vulpian²²). It was not surprising, therefore, to find that the toad's heart is far less sensitive to Apocynamarin than is the frog's heart. In one case a toad's ventricle continued beating for 18 hours in the Locke-Williams apparatus, being perfused for the whole time with 1 : 50,000 Apocynamarin,

the only effect of which was to increase the size of the output with some irregularity towards the end of the prolonged perfusion (Fig. 7); whereas a solution of one-tenth this concentration (1:500,000) rapidly produces systolic arrest of the frog's ventricle. Other toads' hearts also possessed a similar partial immunity to Apocynamarin.

B. EXPERIMENTS ON MAMMALS.

The mammals used were rabbits, cats, dogs, and a monkey.

The animals were fully anaesthetised, except for simple observation of the effects of hypodermic injection or administration by the mouth. The anaesthetics used were usually chloroform followed by ether. In a few experiments in dogs the combination of morphia (0.01 grm. per kilo) hypodermically and paraldehyde (1.5 cc. per kilo) by the stomach tube was employed, a little chloroform being subsequently given by inhalation during the preliminary dissection. The general results have been very similar in the different types.

I. *Observations on the intact animal.*

If a large dose be given by the mouth, e.g., 0.1 grm. to a dog, the chief result is to cause vomiting in a few minutes, which is repeated at intervals for an hour or two, and removes all but traces of the quantity administered from the possibility of absorption. The rapid onset of the vomiting under these conditions suggests that local action on the mucous membrane of the stomach is chiefly responsible. It will be shown later, however, that this is not the only mechanism by which vomiting is induced by the drug. If a dose of 1 or 2 mg. is given by the mouth to a cat vomiting does not usually result. For 15 to 20 minutes, indeed, no result is seen, as a rule. It is then noticed that the pulse is somewhat diminished, and this retardation is gradually accentuated. The heart-beat becomes perceptibly more forcible as the rate decreases. If vomiting occurs with this smaller dosage it usually happens about 30 minutes after the administration.

If the Apocynamarin (or Cynotoxin) is given hypodermically the symptoms appear more rapidly. 1 or 2 mg. injected into a cat caused vomiting in about 10 minutes.

In a large dog injections, amounting to 4 mg. in all, caused pronounced slowing of the pulse with a feeling of increased tension, and a similar result was obtained with a monkey.

The following protocols illustrate these effects:—

(1) Effect of administration by the mouth, continued for 8 days. Cat, male, weighing 2,300 grm.:—

May 6th.

Before any Apocynamarin was given the rate of the heart-beat, when the cat was kept quiet, varied from 200-190 per minute.

3.4 p.m. 2 mg. Apocynamarin in capsule given by mouth.

4.5 p.m. Heart beat 160 per minute. Perceptibly more forcible.

4.30 p.m. Heart-beat 172 per minute, becoming quicker if the cat is excited.

May 7th.

- 9.51 a.m. Cat quite normal. Heart-beat 170 per minute when quiet. 2 mg. Apocynamarin in capsule given by mouth.
 10.20 a.m. Heart-beat 120 per minute. Regular and forcible. No signs of nausea.
 10.22 a.m. Cat suddenly vomited without any premonitory symptoms.
 10.55 a.m. Heart-beat 140 per minute. No further sickness.
 5.10 p.m. Heart-beat 148-152 per minute. Cat appears to be quite well. 2 mg. Apocynamarin in capsule given by mouth.
 5.55 p.m. Heart-beat 100-112 per minute. The animal is quiet.

May 8th.

- 10.20 a.m. Cat appears to be quite well. Heart-beat 140 when the animal is quiet; it becomes a little more rapid after walking about the laboratory.
 10.23 a.m. 2 mg. Apocynamarin in capsule given by mouth.
 10.58 a.m. Heart-beat 128 per minute. No signs of discomfort or uneasiness.
 11.30 a.m. Defaecation and micturition. Heart-beat much the same. No second dose was given on this day.

May 9th.

- 11.45 a.m. Cat seems well. Heart-beat 176-184 per minute.
 11.50 a.m. 2 mg. Apocynamarin in capsule given by mouth.
 12.24 p.m. Heart-beat 144 per minute. No symptoms of discomfort or nausea.
 1.10 p.m. Heart-beat 156 per minute. Micturition.
 3.40 p.m. Heart-beat 148 per minute. Cat seems quite well. 2 mg. Apocynamarin in capsule given by mouth.
 3.45 p.m. Heart-beat 140 per minute.
 4.25-4.35 p.m. Four readings of heart-beat during this period were, 128, 124, 136, 140.

May 10th.

- 9.50 a.m. Heart-beat 148 per minute.
 10.0 a.m. 2 mg. Apocynamarin in capsule given by mouth.
 10.30 a.m. Heart-beat 108 per minute.
 5.0 p.m. Heart-beat 136 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 5.35 p.m. Heart-beat 108-112 per minute.

May 11th.

- 9.55 a.m. Heart-beat 148 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 10.45 a.m. The cat basking in sunlight. Heart-beat 128.
 4.44 p.m. Heart-beat 140 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 6.0 p.m. Heart-beat 108 per minute.

May 12th.

- 5.45 a.m. Cat appears to be quite well. Heart-beat 148 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 5.15 p.m. Heart-beat 148 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 5.58 p.m. Heart-beat 140 per minute.

May 13th.

- 10.0 a.m. Heart-beat 128 per minute when asleep. 148 when disturbed.
 10.26 a.m. 2 mg. Apocynamarin in capsule given by mouth.
 11.20 a.m. Heart-beat 120 per minute.
 2.5 p.m. Heart-beat 144 per minute. 2 mg. Apocynamarin in capsule given by mouth.
 2.25 p.m. Heart-beat 120 per minute.

May 14th.

Heart-beat 148. Cat appears to be quite well. Experiment discontinued.

May 18th.

Heart-beat 150 per minute. Cat appears to be quite normal.

It is clear, then, that, when the drug is repeatedly administered by the mouth in small doses, the pulse rate of the cat, which was normally 180-200 per minute (the normal average of a number of cats was found to be about 180), could be kept down to an average rate of about 140. When the animal was fully under the influence of the drug, from 30 minutes to 3 hours after the administration, the rate fell on several occasions to about 110. This small dose (2 mg.) by the mouth produced vomiting only on one occasion. There was no evidence of any cumulative effect. In fact, on the morning after the day (8th May) on which only one dose was given, the pulse had regained almost its normal rate (176). It soon became again permanently normal when the administration was discontinued. During the period of administration the animal took its food well and rapidly gained weight. When it was killed, 19 days after the commencement of the experiment, no signs of gastric or intestinal irritation were found post mortem.

(2) Cat—Weight 2,810 grm.

The animal was very excitable and the pulse rate continuously above 200.

- 10.5 a.m. Pulse rate 212; counting difficult.
- 10.25 a.m. 1 mg. of Apocynamarin in 2 cc. saline injected hypodermically. Pulse rate practically unaltered, and cat quite normal till
- 10.37 a.m. when vomiting occurred.
- 10.51 a.m. Cat vomited again; much salivation. Pulse 188.
- 11.0 a.m. Cat quiet. Salivation continues. Pulse 148.
- 11.15 a.m. Much collapsed. Respiration very rapid; cat pants with its mouth open.
- 11.23 a.m. Condition the same. Defæcation. Pulse 104 (irregular).
- 11.37 a.m. Condition the same. Pulse 92 (very irregular; intervals of 4 sec. occurred without any beat). Another count of the pulse was 108.
- 11.45 a.m. Condition improving. Pulse more regular but still very slow.
- 12.0 noon Great improvement. Cat walks about. Pulse 160.
- 12.10 p.m. Cat almost normal again. Pulse 186.

From this time no further symptoms occurred, and after effects were absent.

In this experiment the rapid onset of the symptoms and their comparatively short duration indicate a very rapid absorption and excretion or destruction of the drug. The slowing of the pulse was probably delayed by the vomiting. The pronounced retardation first appeared after the vomiting ceased. The panting respiration with the mouth open was probably due to high blood pressure.

(3) Monkey, male, April 27th, 1909—A full grown *Macacus Rhesus*.

- 12.55 p.m. Pulse in femoral artery 188 per minute. 2 mg. Apocynamarin hypodermically
- 1.2 p.m. Pulse in femoral artery, 196 per minute.
- 1.10 p.m. Pulse in femoral artery, 184 per minute. Micturition during slight struggle.
- 1.15 p.m. Pulse in femoral artery, 184 per minute. Micturition during slight struggle.

- 1.25 p.m. A further 2 mg. Apocynamarin hypodermically.
1.29 p.m. Pulse in femoral artery, 168 per minute; less compressible.
1.37 p.m. Pulse in femoral artery, 152 per minute.
1.41 p.m. Pulse in femoral artery, 112 per minute; irregular; drops beats occasionally.
1.44 p.m. Pulse in femoral artery, 96 per minute some counts—others as high as 120.
1.46 p.m. Pulse in femoral artery 107 per minute.
1.47 p.m. Micturition.
1.52 p.m. Pulse in femoral artery, 108 per minute. Put back in cage.
2.30 p.m. Vomited.
3.24 p.m. Pulse rapid and weak, but regular—210 per minute.
3.26 p.m. Breathing slightly wheezy. Râles in chest. Pulse 200 per minute.

Next day it had recovered completely, and is still living and well.

A study of these protocols in detail shows three stages of action on the heart. In the case of the cat to which repeated doses of 2 mg. were given by the mouth, the therapeutic stage of the action is illustrated by the minor degrees of slowing, accompanied by strengthening of the heart-beat. The doses were, however, in most cases absorbed with sufficient rapidity to produce the further stage of excessive retardation, the beat falling in several instances to about 110 per minute and becoming somewhat irregular. This stage of excessive inhibition is illustrated more strikingly in the next protocol, where it is seen that, after 1 mg. hypodermically, the pulse rate sank from over 200 to as low as 92, being at that time markedly irregular. In the case of the monkey, which received 4 mg. hypodermically altogether, this stage of excessive inhibition gave way to the third stage of excessively rapid pulse, from which, however, the animal recovered. These are, of course, the well-known stages of digitalis action, and they have been so completely analysed by Cushny and others that we have contented ourselves with showing that the action of the Apocynum principle follows the same general lines. Before passing, however, to the experiments under anæsthetics, certain other features of the protocols deserve mention. Vomiting and purging have been described as effects of administering Apocynum: on the one hand, they have been regarded as drawbacks to its use as a heart tonic, and, on the other hand, have even led some to advocate the use of the drug as an emetic and cathartic. Using the pure principle we have seen no reason to conclude that Apocynamarin in therapeutic doses is a gastric or intestinal irritant. Vomiting, following an heroic dose, such as 100 mg. of the intensely bitter substance, cannot be regarded as significant. Smaller doses by the mouth produce vomiting, if at all, only after the appearance of action on the heart indicates that absorption has taken place; such vomiting occurs earlier, and far more constantly, if the dose is injected hypodermically. It is clearly, then, an effect produced after absorption, and must be attributed either to an action on the centre, or, possibly, on the musculature of the stomach. Such an action, in producing increased tonus of plain muscle, probably accounts for the defæcation and micturition which, in some cases, followed and appeared to be causally related to the administration. There

was no evidence of irritation of the subcutaneous tissues any more than of the alimentary mucous membrane. It should further be pointed out that we were, in all cases, using hypertherapeutic doses, and it is unlikely that vomiting or purging would result from the use of the pure principle in practical medicine. It seems probable that the irritant effects attributed to extracts of *Apocynum* are due to the presence of some other constituents than the active principle. Such experiments as we have made with various crude extracts lend support to this conclusion.

Such small variations of respiratory movements as we observed may probably be regarded as secondary to changes in the blood pressure. In a few cases, especially in those in which nausea and vomiting were prominent features, moist sounds were audible on auscultation of the chest. These are probably attributable to a reflex hypersecretion, secondary to the nausea, and comparable to that produced by Squill.

II. *Experiments under anæsthetics.*

The three stages described above, with a further stage leading to death, can be well seen in records of the arterial blood pressure from an anæsthetised animal which has received a hypodermic injection of 5 to 6 mg. of the active principle. In the first stage it can be seen that moderate slowing of the heart is accompanied by rise of blood pressure. In the second stage, which cannot always be clearly differentiated, the heart-beat becomes often so slow that the blood pressure falls below the initial level, in spite of the peripheral arterial constriction to which we shall refer later. Sooner or later the retardation disappears and the heart-beat becomes extremely rapid, the blood pressure rising continuously. The change may take place abruptly, as in Fig. 8. Later the blood pressure shows marked fluctuations corresponding to irregular output of the ventricle. A fall of the blood pressure to zero, which is frequently quite sudden, indicates failure of the heart-beat, and post mortem the left ventricle is found in systolic contraction, the systole of the right ventricle being masked by engorgement. The degree of systole of the left ventricle varies, but is usually complete after such doses as that indicated. The different stages are shown in Fig. 8. Fig. 9 illustrates the second stage of excessive vagus inhibition.

If the drug is injected intravenously the same sequence of stages can be seen, but they follow one another more rapidly, and are less easily differentiated, so that, as described by Cushny³, with other members of the digitalis series injected intravenously, the main distinction which can be drawn is between a first stage in which the beat is slowed by inhibition, and a second in which the heart escapes from inhibition, becomes very rapid and then irregular, and stops in systole.

The interpretation of the different stages is easily made on familiar lines. The retardation of the heart-beat in the earlier stages is eliminated by

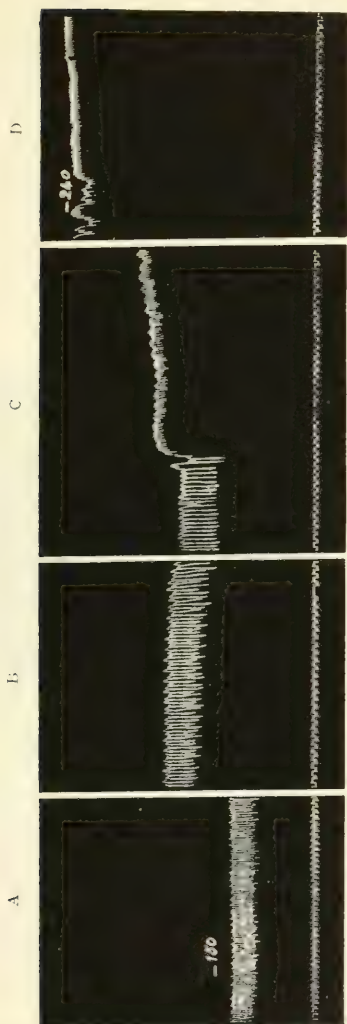


Fig. 8. γ linear. Cat. 1,800 gms. ether. Circled blood pressure. Four stages of the action of 4.5 mg. Cynotossin, injected hypodermically. A—Normal. B—12 minutes after the injection. C—6 minutes later. D—3 minutes later.

destruction of the medullary centres, by section of the vagi, or by administration of atropine. The fact that, in the early stages of the action of the drug on the isolated heart, a very slight slowing accompanies the increase in amplitude* suggests that there may be a slight action on the peripheral inhibitory mechanism, as has been stated in the case of other members of the digitalis series. This action, however, is of altogether subordinate importance to the effect through the centre, and the effect of cutting the vagi is almost equivalent to giving atropine as regards the elimination of the inhibitory effect. The quickening of the rhythm, accompanied by rise of blood pressure, in the third stage is clearly due to escape from the inhibition. We have found no evidence to support Wood's statement that actual paralysis of the vagus mechanism occurs. Sokoloff²³ pointed out that with Apocynum, as with Digitalis, a further injection in the stage of acceleration causes a temporary renewal of the inhibition. We have ourselves observed

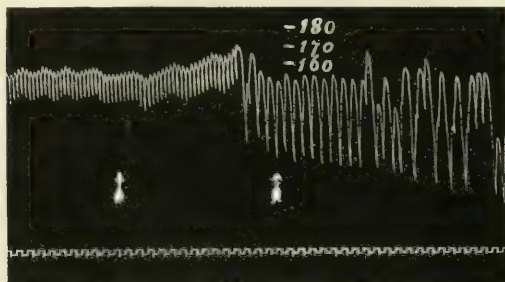


Fig. 9. $\times \frac{1}{3}$ linear. Cat. 3,592 grm., ether. 1 mg. Cynotoxin injected intravenously between



that electrical stimulation of one vagus quite late in this third stage is still capable of producing a distinct slowing of the beat accompanied by fall of blood pressure. The explanation originally advanced by Cushny³, and more recently adopted by Lhotak von Lhota¹⁵, for the escape from vagus inhibition of hearts poisoned by other members of the digitalis series, may be applied to this case also. The heart muscle becomes so excitable that the impulses which reach it through the vagus mechanism are no longer adequate to produce an obvious retardation. They are not, however, without effect, for we have convinced ourselves that the heart passes more rapidly into fatal delirium when the vagi are cut, or when atropine has been injected, than when the inhibitory mechanism is left intact.

* An actual count made on the record reproduced in Fig. 17, shows 53 beats before, 51 shortly after the beginning of the drug's action in equal time intervals.

Nature of the effects on the circulatory system.

In analysing the rise of blood pressure during the later stages of the action, two factors have to be taken into account—increased peripheral resistance due to vaso-constriction, and increased output of the ventricles.

Action on plain muscle.

The occurrence of very pronounced vaso-constriction can be detected without graphic appliances; mere inspection of the exposed intestines, which become extremely pale during the rise of pressure following injection, is sufficient to show that vaso-constriction not only occurs, but is so intense that it must play a large part in the production of the rise of pressure. Plethysmographic records indicate the same. Fig 10 shows such a record from

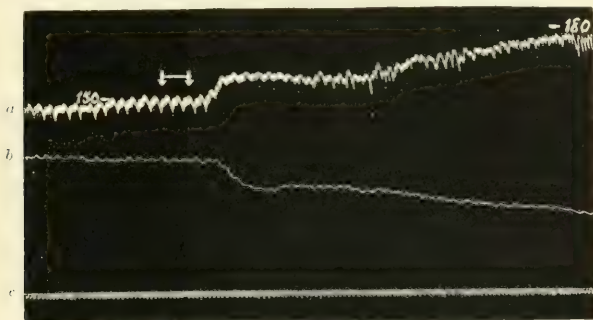


Fig. 10. $\times \frac{1}{2}$ linear. Cat. Ether. (a) Carotid blood pressure. (b) Intestinal plethysmograph. (c) Time in seconds. Between \uparrow — \uparrow 0.5 mg. Cynotoxin injected intravenously.

a loop of intestine. We have found nothing to support Sokoloff's statement that the action is produced by stimulation of the medullary vaso-motor centre, or of the spinal cord. Destruction of the whole brain and spinal cord did not, in our experiments, diminish the vaso-constrictor action. On the contrary, by reducing the arterial tone and blood pressure to a low initial level, this procedure made the effect of Apocynamarin or Cynotoxin more striking, the pronounced vaso-constriction which it produced, together with the alteration in the heart-beat, causing a sudden rush of the blood pressure from its low level to the maximum, as soon as the drug was injected (Fig. 11). Nor is the action on any nervous structure between the spinal cord and the arterial musculature, since, after doses of ergotoxine sufficient to abolish the

vaso-constrictor effect of adrenaline, which now produced only a fall of blood pressure, the vaso-constrictor effect of Apocynamarin was unimpaired, as could be seen from the rise of blood pressure and the pallor of the intestines which it still produced. Measurement of the rate of outflow from the coronary vessels of hearts perfused by Langendorff's method show that marked constriction of these vessels also is produced by Apocynamarin and Cynotoxin. Since there is no clear evidence of the possession of a vaso-constrictor nerve supply by these vessels this fact points again to the action of the principle being on the actual plain muscle of the arteries. In this respect our conclusions are in agreement with those of Wood²⁶, and differ



Fig. 11. $\times \frac{1}{2}$ linear. Cat. Cervical cord cut and brain destroyed. Artificial respiration. Carotid blood pressure. Time in 10 sec. 2.5 mg. Apocynamarin injected intravenously.

from these of Sokoloff²³. Other organs containing plain muscle are similarly affected, contraction of the muscular walls of the stomach intestine, urinary bladder, spleen, and uterus being produced. Fig. 12 shows the effect of adding 1 mg. of Apocynamarin to 250 cc. of warm oxygenated Ringer's solution in which a short length of rabbit's jejunum was suspended so as to pull on a recording lever. Fig. 13 shows the effect of the same dose on the isolated horn of a cat's uterus under identical conditions. In both cases it is seen that the tonus is increased to such an extent as practically to obliterate

the spontaneous rhythm. Contraction of the spleen was shown in plethysmographic records, and in one case wide, rhythmic variations of volume appeared, quite independent of the blood pressure. Intense tonic contraction of the urinary bladder is caused by intravenous injections, and, after

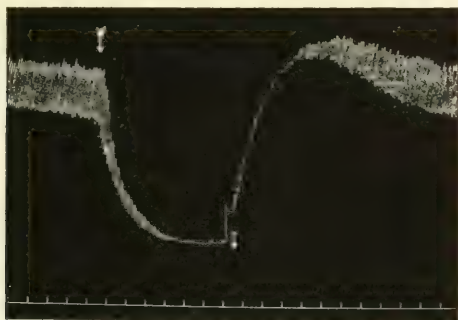


Fig. 12. $\times \frac{1}{2}$ linear. Isolated loop of rabbit's jejunum. Downstroke of lever = contraction. At \downarrow 1 mg. Apocynamarin added to the 250 cc. of warm oxygenated Ringer's solution in which the loop was suspended. At \uparrow change to pure Ringer.

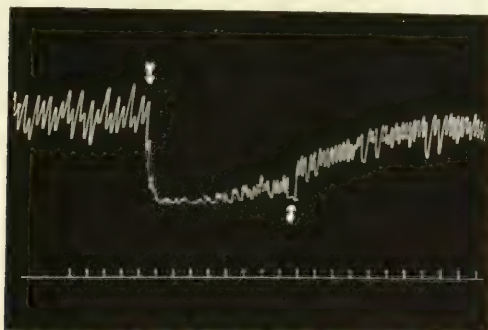


Fig. 13. $\times \frac{1}{2}$ linear. Isolated horn of cat's uterus (non-pregnant). Conditions as in Fig. 12. At \downarrow added 1 mg. Apocynamarin; at \uparrow change to pure Ringer.

a large intravenous injection, the lumen was practically obliterated. The effect on the peripheral arteries is, therefore, merely one instance of the general stimulation of plain muscle fibres.

Action on the heart.

For studying changes in the output of the heart some form of cardiometer would appear to be the ideal instrument. Some of the defects of Roy and Adami's instrument have been indicated by Cushny³, who pointed out that a decrease in ventricular volume may be masked by simultaneous engorgement of the auricle. This objection would be overcome by using an instrument which enclosed the ventricle only. Such can be made, and has been used by several observers, by covering the end of a thistle-funnel with thin rubber, burning a central hole, and pushing the annular rubber diaphragm thus formed over the ventricles, so that its edge grips the auriculo-ventricular ring. We failed to adjust this instrument so as to exclude, at the same time, leakage and hampering of the heart's action. In several cases, when the instrument seemed successfully adjusted, injection of Apocynamarin produced a surprisingly small effect both on the cardiometer record and the blood pressure. In such cases withdrawal of the instrument was succeeded immediately by the rise of blood pressure characteristic of the action of the drug. We were more successful with a simple thistle-funnel slipped inside the opened pericardium, which was tied securely round the rim. The record shown in Fig. 14 was thus obtained, a small Brodie's bellows being the

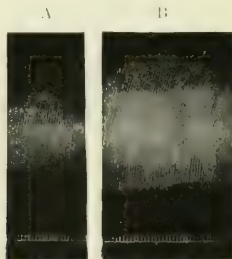


Fig. 14. $\times \frac{1}{2}$ linear. Cat. Cardiometer-record of ventricular volume. A—Normal. B—After injection of 0.5 mg. Apocynamarin.

recording instrument. Though we were able thus to demonstrate directly the increase of output, the cardiometer, in our hands, proved less suitable for following the effect of the drug on the heart through its various stages, for a very small difference in the adjustment is sufficient to vitiate the record completely. For this purpose we found methods which recorded the muscular contraction of the heart wall much more suitable.

The course of events is so clearly similar to that described for other members of the digitalis series that we contented ourselves with recording

contractions of the ventricles, since there is little room for doubt that Cushny's² analysis of the effect of various members of the series on different chambers of the heart will apply to this case also. We recorded the contractions of the dog's left ventricle, *in situ* by means of Cushny's modification of the Roy-Adami myocardiograph, and of the left ventricle in isolated perfused hearts of cats and rabbits by the ordinary method of suspending from the aorta, and connecting the lever to a hook in the tip of the left ventricle. In the experiments on dogs, which were anaesthetised with morphia and paraldehyde, a little chloroform being added during the operative preparation, the blood pressure was also recorded from the carotid artery. Fig. 15 shows samples of a continuous myocardiographic record, the

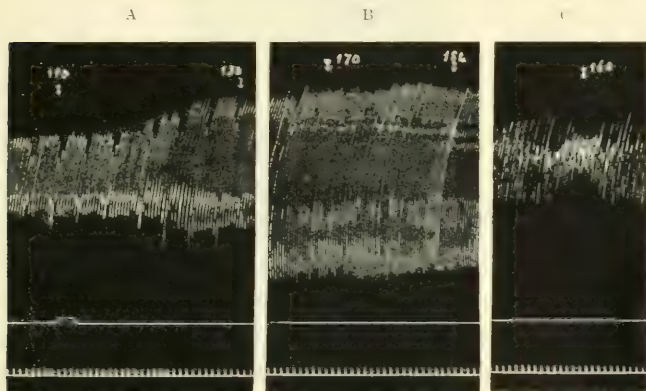


Fig. 15. $\times \frac{1}{2}$ linear. Dog (5½ kilos.). Morphia and paraldehyde. Chloroform. Myocardiographic record. Injection of 2 mg. of Apocynamarin intravenously. Time — 2 sec. A—Before and just after injection. B—36 sec. later than end of A. C—96 sec. later than end of B.

changes in blood pressure being indicated by the figures placed above the tracing. In this instance the preliminary slowing is almost absent though the vagi were intact. Probably the cardio-inhibitory centre was greatly depressed by the anaesthetic. The apparent periodic irregularities in the ventricular tracing before the injection of Apocynamarin were due to the artificial respiration. It will be seen that the injection of Apocynamarin caused, from the first, increase both of diastolic relaxation and of systolic contraction. As the systole continues to gain in vigour the respiratory undulations become less marked. Section (B) of the tracing shows the period of maximum cardiac efficiency under the action of Apocynamarin, systole and diastole being both increased, and the rhythm accelerated, but as yet

perfectly regular. It will be seen that during this period the blood pressure rose from the original 110 to 184 mm. Period (C) shows a later stage where the contractions have become irregular and weak, diastole and systole being both imperfect. Fig. 16 from a similar experiment shows the stage of un-

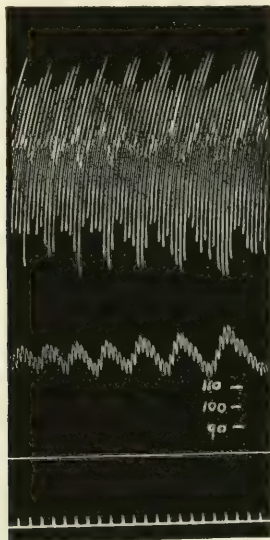


FIG. 16. — Linear. From an experiment similar to that of Fig. 15, to illustrate the stage of undulatory blood pressure.

dulatory blood pressure, the undulations corresponding to rhythmic variations in the amplitude of the ventricular contractions. The condition, which has been the subject of elaborate analysis by Cushing¹, and has been produced by him by other means of excitation as well as by digitalis poisoning, is preliminary to the stage of delirious irregularity. The undulations of blood pressure, which are usually very regular when they first appear, may disappear for a time, the heart-beat becoming temporarily uniform, and may then reappear with a different rhythm. They are well seen in cardiometric as well as in myocardiographic records. These rhythmic variations have been shown by Cushing to be due to the acquisition by the excessively excited ventricle of a rhythm of its own, independent of that of the auricle. In his earlier paper he regarded the variations as being due to the interference in each chamber of the two rhythms, that initiated in the chamber itself and

that transmitted from the other. A maximum ventricular beat would occur when a transmitted impulse from the auricle coincided with an impulse originating in the ventricle itself; a minimum beat, when the transmitted impulse fell wholly within a refractory period of the idioventricular rhythm. A similar explanation applied to the rhythmic variation of auricular contractions. In a later paper¹, dealing wholly with this phenomenon, Cushny states that he has been able to induce it after destroying conductivity between auricle and ventricle, and attributes it to a periodicity in the filling of the ventricle by the auricular systole. This would be more complete as the auricular systole approached its normal relation to the ventricular systole, and less complete as it diverged from this. Since the two rhythms, though different, are both regular, there will be a regular recurrence of the optimum relation of the two, giving a maximal ventricular output. The auricular periodicity is similarly explained by a rhythmic variation in the freedom of the flow of blood into the ventricle.*

It cannot be doubted that this later theory offers an adequate explanation of the phenomenon as seen in the heart in its natural relations. On the other hand, it clearly fails to explain the occurrence of the rhythm in the ventricular contractions of the isolated perfused heart. Fig. 17 shows that, in such a heart, perfused with Ringer's solution containing Cynotoxin in high dilution, the ventricular contractions present this periodicity in a very marked form in the stage of action preceding delirium. Under such conditions the left auricle, at least, is quite empty, and the phenomenon can have no connection with the filling of the ventricle. This observation suggests that the interference of excitation waves, in accordance with Cushny's earlier explanation, is a sufficient cause of the periodicity, though the filling of the ventricle may also be concerned when the heart is in its normal relation. Possibly a simultaneous record of auricular and ventricular contractions on the isolated, perfused heart would throw further light on the subject.

The records from isolated hearts, for the perfusion of which Locke's method was used, correspond also in other respects closely with those obtained with the myocardiograph. The final systole, as might be expected from the fact that interior of the ventricle is exposed to no increasing pressure, is more complete than that usually seen in an animal killed by the drug.

Diuretic action.

The clinical accounts of the action of Apocynum emphasises its diuretic action, and its consequent value in dropsy. It has even been called the "vegetable trocar" (cp. Dabney²).

Though the diuretic action of the drugs of the digitalis series is a familiar clinical phenomenon, many experimental investigations of the effect have

* The same phenomenon has quite recently been studied by Straschewski³, whose conclusions as to its cause are practically identical with those of Cushny's later paper.

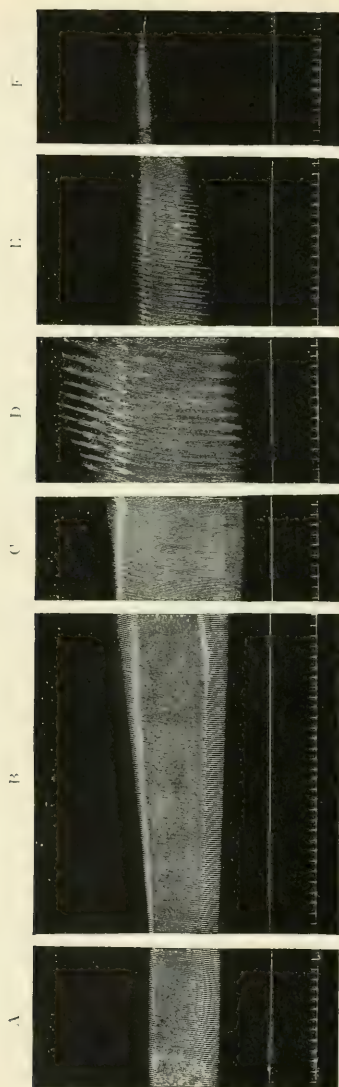


Fig. 17. $\frac{1}{2}$ linear. Isolated heart of Cat, perfused with oxygenated Locke-Ringer solution. Upstroke = systole.
 Time = 2 sec. A Normal. B—Just after change to 1 : 150,000 Cynoxin. C—52 sec. after end of B.
 D—112 sec. after end of C (note ventricular inflections). E—136 sec. after end of D. F—110 sec. after end
 of E.

yielded results not immediately accordant with the clinical observation. Bradford and Phillips¹, and Gottlieb and Magnus¹¹ found that the kidney vessels did not escape the general vaso-constrictor effect of this drug, and Brunton and Power², Pfaff¹¹, and Marshall¹⁷, all found that diuresis was decreased by the large doses which they administered. It has recently been pointed out by Jonescu and Loewi¹¹ that therapeutic doses of these drugs produce but the slightest, if any, rise of the normal blood pressure, but that they, nevertheless, produce, especially in rabbits, a greatly increased diuresis, accompanied by increased kidney volume.

Our experience with Apocynamarin has been, on the whole, of a similar nature. In the cat and dog large doses (1 mg. or more) intravenously cause a primary diminution of the flow of urine, which usually, however, gives way to acceleration. The kidney volume diminishes during the initial retardation of the urine flow, to increase again beyond the original as the secondary acceleration occurs. If the drug is very slowly absorbed after subcutaneous injection it is possible to observe a considerable increase in the flow of urine, even though cardiac inhibition prevents the rise of the blood pressure beyond the initial level. Fig. 18 illustrates such a condition in an experiment on a cat.

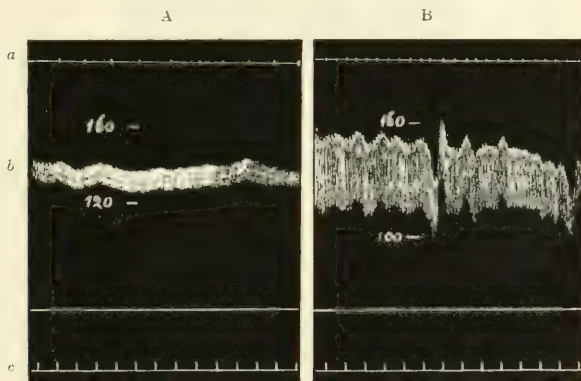


Fig. 18. $\times \frac{1}{2}$ linear. Cat. Chloroform and ether. (a) Drop record of urinary secretion (bladder cannula); (b) Carotid blood pressure; (c) Time in 10 sec.. A—Normal. B—6 minutes 40 sec. after hypodermic injection of 2 mg. Apocynamarin.

We found, also, in accordance with the statements of Pfaff and of Jonescu and Loewi, concerning the digitalis drugs, that the rabbit is far more sensitive to the diuretic effect of small doses of Apocynamarin than the dog or cat. Fig. 19 shows the effect of intravenous injection of 0.5 mg. of Apocynamarin on the flow of urine and kidney volume in this animal. One other point deserves mention. It has been mentioned by Pfaff, and by Jonescu and

Loewi, that, after an injection of Digitalis, even when this of itself produced no diuresis, as is frequently the case in the dog, a subsequent injection of Caffeine, which of itself has also unusually little effect in the dog, produces a profuse diuresis. In the case of Apocynamarin the converse seems also to be true. In a rabbit, after an injection of Caffeine which was in itself but feebly diuretic, an injection of Apocynamarin produced a diuresis far more

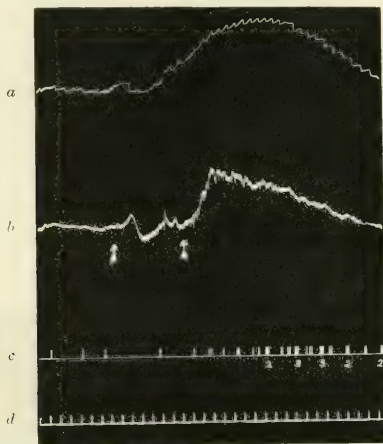


Fig. 19. $\times \frac{2}{3}$ linear. Rabbit. Urethane. (a) Kidney volume; (b) Carotid blood pressure; (c) Drop record of urine flow, and zero of blood pressure; (d) Time in 10 sec.. Between \uparrow — \uparrow 0.5 mg. Apocynamarin injected intravenously.

profuse than could be accounted for by the addition of the effects which the two drugs would separately produce. This appears to be one of the rare instances where polypharmacy has an experimental, though not, as yet, a completely rational basis, and deserves further investigation.

Excretion.

Attempts were made to detect by physiological tests the presence of Apocynamarin in the urine from the cat which received two doses of 2 mg. *per diem* by the mouth for eight days. Three separate samples of urine were used, but all gave negative results. The question as to whether it is excreted as such, or destroyed in the body, must, therefore, remain open, though the negative evidence is, on the whole, in favour of the latter.

CONCLUSIONS.

It is clear that the characteristic effects of the two species of Apocynum under consideration are due to the bitter principles named Cynotoxin and Apocynamarin by their respective discoverers. There is no pharmacological indication of any difference between the two. The action is in all respects a characteristic digitalis effect. Careful quantitative comparison with other pure principles would be needed to establish the position of the drug in the digitalis series. We have only determined that its vaso-constrictor action is considerably more powerful than that of Strophanthin: its action on the heart seems but little weaker than that of the latter. Its diuretic effect seems to be similar to that of other drugs of the series. On the other hand it appears to be excreted or destroyed with comparative rapidity, and there seems to be experimental basis for the statement that Apocynum is not cumulative in its action. This fact should tell in favour of the use of Apocynum in practical therapeutics, and the employment of the pure active principle should eliminate the drawbacks which have hitherto restricted its use, and which seem to be due to the presence of other constituents of an irritant nature in the crude extracts. We have observed no irritant effects with either oral or subcutaneous administration of the pure principles. The rapidity of the action enjoins caution with regard to subcutaneous dosage.

It is a pleasure to acknowledge our indebtedness to Messrs. Finnemore and Moore for the specimens of active principles: also to Dr. F. B. Power for kindly criticising our account of the chemical investigations.

SUMMARY.

1. Crystalline Apocynin (Acetovanillone) has but the feeblest physiological action when pure.

2. The true active principle of Apocynum is a definite crystalline non-glucosidal substance, to which the names "Cynotoxin" and "Apocynamarin" were given by the investigators who independently obtained it from *A. cannabinum* and *A. androsaemifolium* respectively. Its action is in all respects that of the digitalis series, but its effect is apparently not cumulative.

BIBLIOGRAPHY.

- BRADFORD and PHILLIPS. Journ. of Physiol., 1887, viii, 117.
- BRUNTON and POWER. Proc. Roy. Soc., 1874, xxii, 420.
- CUSHNY. Journ. of Exper. Med., 1897, ii, 233.
- CUSHNY. Journ. of Physiol., 1899, xxv, 49.

- ⁵ DABNEY. *Therap. Gazette*, 1898, xxii, 730.
- ⁶ DIXON. *Journ. of Physiol. (Proc. Phys. Soc.)*, 1907, xxxv, 26.
- ⁷ DIXON. *Journ. of Physiol.*, 1902, xxviii, 57.
- ⁸ FAUST. *Archiv f. exper. Path. u. Pharmak.*, 1902, xlvii, 278.
- ⁹ FINNEMORE. *Trans. Chem. Soc.*, 1908, xciii, 1513.
- ¹⁰ FINNEMORE. *Proc. Chem. Soc.*, 1909, xxv, 77.
- ¹¹ GOTTLIEB and MAGNUS. *Archiv f. exper. Path. u. Pharmak.*, 1902, xlvii, 135.
- ¹² GRISCOM. *Amer. Journ. Med. Sci.*, 1833, xii, 53.
- ¹³ HUSEMANN. *Archiv f. exper. Path. u. Pharmak.*, 1876, v, 245.
- ¹⁴ JONESCU and LOEWI. *Archiv f. exper. Path. u. Pharmak.*, 1908, lix, 71.
- ¹⁵ LHOTAK VON LHOTA. *Archiv f. exper. Path. u. Pharmak.*, 1908, lviii, 350.
- ¹⁶ LOCKE and ROSENHEIM. *Journ. of Physiol.*, 1907, xxxvi, 205.
- ¹⁷ MARSHALL. *Journ. of Physiol.*, 1897, xxii, 1.
- ¹⁸ MOORE. *Trans. Chem. Soc.*, 1909, xciv, 734.
- ¹⁹ MURRAY. *Therap. Gazette*, 1889, xiii, 585.
- ²⁰ PHISALIX and BERTRAND. *Archiv de Physiol. norm. et pathol.*, fifth series, 1893, v, 511.
- ²¹ PFAFF. *Archiv f. exper. Path. u. Pharmak.*, 1893, xxxii, 1.
- ²² SCHMIEDEBERG. *Therap. Gazette*, 1883, xvi, 161.
- ²³ SOKOLOFF. *Abstract in Med. Chronicle*, 1888, viii, 466. (Russian original—*Ejenedelnaia klinitscheskaia Gazeta*, 1888, 507.)
- ²⁴ STRASCESKO. *Archiv f. d. ges. Physiol.*, 1909, cxxviii, 1.
- ²⁵ VULPIAN. *C. R. Soc. de Biol.*, second series, 1856, iii, 125.
- ²⁶ WOOD (H. C., Jr.). *Journ. Amer. Med. Assoc.*, 1904.

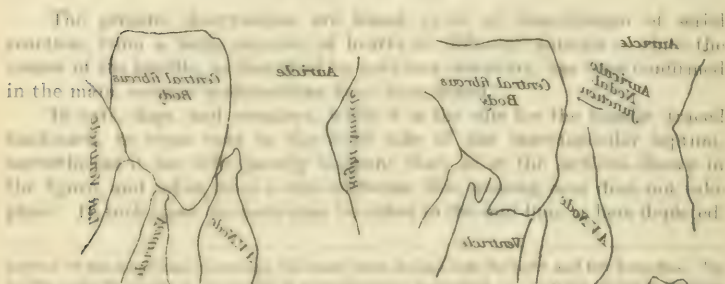
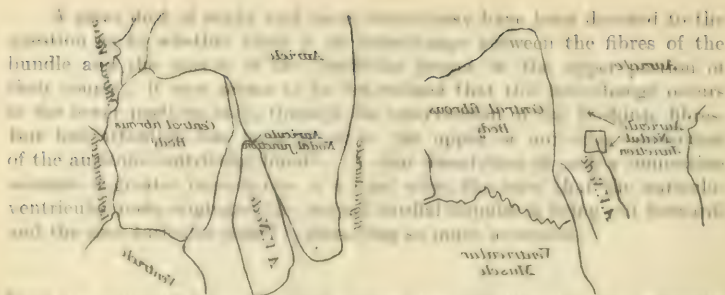
ON THE AURICULO-NODAL JUNCTION.

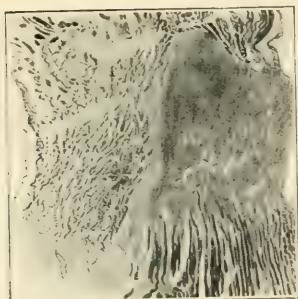
By ALFRED E. COHN.

(New York.)

SINCE the announcement by Gaskell¹ in 1883 of the theory of stimulus transmission from auricle to ventricle, the endeavour to discover the anatomical pathway over which stimuli could be propagated, has been persistent. The investigations which have been made have demonstrated the existence of a pathway of muscular fibres and, by experiment, have shown its physiological significance. Paladino² is reported by Bardeleben to have been the first to find such a connection, but, according to Retzer, who examined the evidence, there is no mention of the fact in Paladino's paper. In 1892, nine years after Gaskell's paper, Kent³ first reported the presence of this muscular connection, together with experiments, in which he used a clamp (p. 250), while His (Jr.),⁴ soon afterwards published his results independently, citing experiments to substantiate his discovery of a definite bundle of fibres. In the course of the following years, His added more evidence to his view of the subject, but nothing further was done until, in 1904, both Retzer⁵ and Braeunig⁶ substantiated Kent's and His's observations. There the matter rested until, in 1906, Tawara⁷ described in elaborate detail what was known at that time, and showed that the Purkinje fibres represented the end-branches of the auriculo-ventricular bundle. He also described the A-V node, to which his name has since been attached, as a localized swelling on the bundle consisting of a close interlacement of fibres, and made clear the origin, course, and endings of the whole system. Soon after, in 1906, Keith and Flack⁸, and Fahr⁹ (in part) substantiated these views, while in 1908 Mönckeberg¹⁰ in a large monograph, amplified them, and described the pathological changes in the bundle noted up to that date. The unusual glycogen content of the Purkinje fibres was first described by Marchand¹¹, and later by Aschoff for Nagayo¹ in 1908. References to details of these matters are to be found in Tawara's and Mönckeberg's monographs*.

* The course of the auriculo-ventricular bundle is as follows: Its fibres take their origin from the auricular musculature, as set forth in the present paper, and pass forward to form the node of Tawara at the lower edge of the auricular muscle. In most mammals the bundle then proceeds forward and somewhat upward and usually to the left, passing to the right of the central fibrous body. Then it passes forward in the *pars membranacea septi*, the lower part of which it perforates, usually nearer the left than the right side, but subject to considerable variation. At the anterior

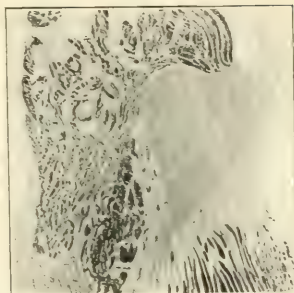




M. H. Lumsden

FIG. 1.

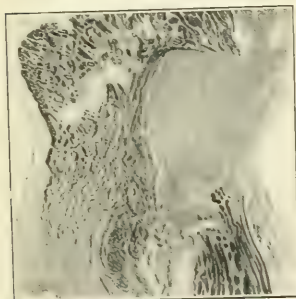
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FIG. 2.

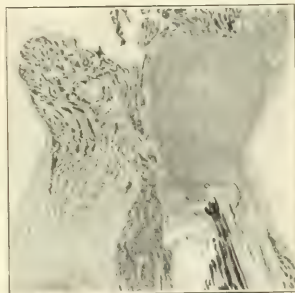
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FIG. 3.

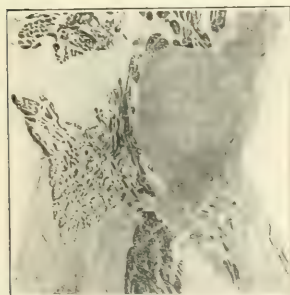
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FIG. 4.

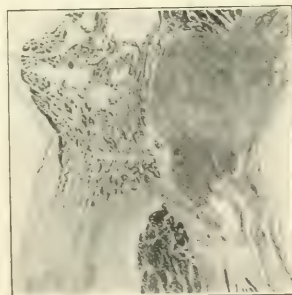
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FIG. 5.

17-4



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FIG. 6.

17-3

Figs. 1 to 6. The figures show the gradual separation from auricular musculature of fibres which form the auriculo-nodal junction (Fig. 1); the transition (Figs. 2 and 3) of these into those of the auriculo-ventricular node; and the complete separation (Figs. 4 and 5) of the auriculo-ventricular node, and the beginning of the passage ventrally to form the auriculo-ventricular bundle (Fig. 6). The drawings are made from a series of sections of the septum of a heart of a *Cercopithecus* (magnification 25 diam.). The top of each figure is dorsal, the bottom ventral.

or even nearer the left side. These variations of position probably depend on the embryological history of the individual case, and are the outcome of the topographical condition in which the upper connection of the primitive auricular canal is left after its invagination into the ventricle, and the changes subsequently wrought in the formation of the interauricular and interventricular septum (Retzer¹¹), by the joining of the upper, intermediate, and inferior embryological septa.

It can readily be imagined that during its development, the auricle may come to lie somewhat lower in relation to the ventricle, so that the auriculo-ventricular junction, instead of passing horizontally in the septum, lies somewhat obliquely, the line passing from the left side downward to the right, a condition not infrequently seen and not to be explained by an inclined plane of the sections. Another variation which may occur is that the auricular union with the bundle takes place, rarely it seems, at a point rather far forward in its course. These two variations in the embryology may well account for several of the atypical anatomical appearances in the neighbourhood of the *pars membranacea septi*. The bundle begins at the auriculo-ventricular node, and in its passage forward and to the left, curves somewhat upward at first, and subsequently downward: in other words, it is convex upwards. The height of the curve in any instance will depend on the position in which the lowest portion of the auricle (where the nodal junction is made) is left in relation to the ventricle after the invagination of the auricular canal: the more oblique the auriculo-ventricular junction, the greater will be the convexity of the curve, and the lower will the node appear to lie.

It follows from these considerations that the point or points of the node, from which fibres of communication to the auricle arise, must vary in different hearts according as the position of the node varies in its relation to the course of the bundle and the auricle. If, as is usually the case, the course is horizontal, the junction fibres lie behind and to the right. If it is curved, with its convexity upward, they will come off posteriorly, from below, and from both sides, considering the node as ovoid or cubical in shape. As to whether they arise on the left side seems to depend on whether the node lies near the median line or on the left rather than on the right of the septum.

THE AURICULO-NODAL JUNCTION.

In the first reports of the communications of the bundle, by Kent, the localisation of the bundle or bundles is vague, and the course is not clearly described. A description of the nature of the auricular connection is entirely wanting. His (p. 23)* describes the anatomy as follows:—"The

* He gives no account of how the junction between auricle and bundle is effected, while two errors are manifest: first, the assertion that the auriculo-ventricular bundle begins in the posterior wall of the right auricle, whereas the actual starting point is in the floor of the coronary sinus; and second, the assertion that there is an exchange of fibres at the upper edge of the ventricular septum with ventricular muscle (an error also made by Retzer).

bundle arises at the posterior wall of the right auricle. Near the interauricular septum in the atrioventricular groove, it lies on the upper edge of the interventricular septum, with which it exchanges fibres."

Retzer (p. 8) in his description says that "the connective tissue disappears entirely (from between the auriculo-ventricular bundle and the auricle), and the bundle can no longer be separated from the rest of the musculature (Fig. 8), especially since the course of the fibres is the same as those of the auricle." There is also a further reference (p. 13), and the final observation "that in his series the bundle at its origin unites completely with the auricular musculature, so that no further details as to its course can be given" (i.e., its course to the posterior wall of the right auricle, which His describes).

Braeunig writes (p. 17): "At the point where the musculature of the auricle (right) is bounded by the connective tissue of the atrioventricular groove, two processes of connective tissue pass upward and to the right into the muscle. The portion of the bundle which lies between these connective tissue strands, and which is separated by them from the rest of the musculature, passes forward into the connective tissue of the auriculo-ventricular groove. This separation of muscle (from auricle by connective tissue) becomes progressively clearer in succeeding sections, until the bundle, entirely separated from auricular muscle, comes to be entirely surrounded by connective tissue."

Tawara describes the junction between auricle and node a number of times (for the dog at pp. 15, 19, 22; for man at pp. 38, 44, 53; for cats at p. 72; for sheep at pp. 78, 80, 98; and for the calf at p. 100). His detailed descriptions refer to the dog's heart. In the sheep's heart (p. 128) he does not find that all the fibres of the node pass into the auricular muscle; some end blindly in the connective tissue and fat which separate them, an appearance attributed by him to the fact that in his series every section was not mounted. It is usually only at the right side that the node is *bounded* by auricular muscle. Dense fatty tissue, through which only occasional single strands of muscle fibres pass, surrounds the auricular end of it on all the other sides. Three methods of junction are noted (Plate IV, Fig. 6): (a) where several node fibres form one auricular fibre; (b) where a small node fibre enters an auricular fibre obliquely; and (c) where star-like masses are formed by the convergence of several fibres.

The description in the dog (p. 136) which answers at the same time for man is more complete. Here the connection is made by the so-called posterior portion of the auricular division of the auriculo-ventricular system, the anterior portion being the node. The fibres of communication arise from the dorsal and right portions of the node; they are small and do not interlace as in the node, but run parallel, usually in small bundles separated by masses of connective tissue. They run almost to the floor of the coronary sinus, and are the fibre-bundles which form the junction with auricular muscle. Tawara emphasizes the fact that the connection is with the dorsal

and right side, while the left, upper, and under sides are surrounded by fat and connective tissue. Histologically the fibres of communication pass over gradually and imperceptibly into auricular fibres, a point being reached where their assimilation to the type of auricular fibre is complete. There is no detailed description for the cat or rabbit. For the human heart he says of one case (p. 38), "the fibres connect in their posterior and right parts with the adjoining auricular muscle"; of another (p. 44), that the bundle fibres "are not so sharply separated from true auricular muscle"; and, finally, of a third (p. 53), that the bundle fibres "cannot be sharply separated from auricular muscle, but on the contrary are connected with the latter."

Keith and Flack merely observe that "traced backwards the bundle is seen to perforate the central fibrous body of the heart . . . so as to show the bundle joining with the fibres of the right auricle."

Fahr is more definite. He says: "Long thin muscle fibres pass through the fatty tissue (which surrounds the bundle), and these represent the connection between auriculo-ventricular bundle and auricular muscle. The connection on the auricular side between bundle and heart muscle is, therefore, not very intimate, for the bundle runs a considerable distance obviously in a pathway of its own . . ." (p. 572).

After mentioning the posterior connection repeatedly, Mönckeberg states his conclusions (p. 90), referring to the human heart only. He agrees with Tawara's observations in the main. Mönckeberg, however, maintains that beside connections on the dorsal and right sides, these exist also above, below, and in front.

The observations in this paper were based on studies made in cats, rabbits, monkeys, dogs, and goats. The portion of the *septum ventriculorum* examined, was cut in a coronal plane perpendicular to the long axis of the heart. The sections, with the exception of those in a few of the dogs, were all cut at a thickness of 8 micra, and every fifth section was mounted. The stain used was Iron Hæmatoxylin, and the counter stain Picric Acid—Acid Fuchsin.

The junction was clearly present in all the animals examined in the present series, though the number of fibres which form the communication varies. There may be a great many, closely packed together, the strands separated by masses of connective tissue; or there may be but a few rather thinner fibres with only delicate connective tissue strands between. It may be that the amount of connective tissue varies with the age of the animal, even though the muscle of the bundle, as Mönckeberg points out, shows little tendency to increase in amount from birth to old age. From what we know of the main stem of the bundle such differences in the quantity of muscle fibre is not surprising. The important point is that this connection between auricle and the node of Tawara is a constant feature.

In *cats* the posterior connection shows considerable variation. The auriculo-ventricular node is often no thicker than the bundle itself, and presents a plexiform arrangement of small fibres within a circumference

equal to that of the main stem. In other instances a distinct enlargement is present. The fibres of the dorsal portion of the node assume a parallel course, become thicker, and pass very gradually into auricular fibres. Sometimes two or more of the smaller fibres unite to form an auricular fibre; sometimes the transition is made fibre by fibre. On approaching the auricle the number of nuclei markedly diminishes, the auricular fibres proper showing relatively few. In node fibres proper, on the other hand, striation of the fibres is rarely seen, while in the transition fibres it comes out clearly, and is fully developed in the auricular fibres.

The position of the node and the transition varies; it may be placed on the left side or in the median line of the septum, though its usual position is on the right side either directly under the endocardium or separated from it by a thin layer of auricular muscle. The size of the central fibrous body seems to be one of the factors determining this variation. On the position of the node depends also the direction in which the transition fibres spread. Usually this is toward the right and dorsally, but they may pass to the left if the node is mesially placed, or on the left side. Fibres may also come off from beneath.

The auriculo-nodal junction in the *rabbit* is constituted in the same way as that in cats. Allowing for the difference in size and the greater paucity of fibres, the description given for them suffices.

In the *monkey* the fibres which compose the node are narrower as compared with auricular fibres. They possess relatively larger nuclei, which

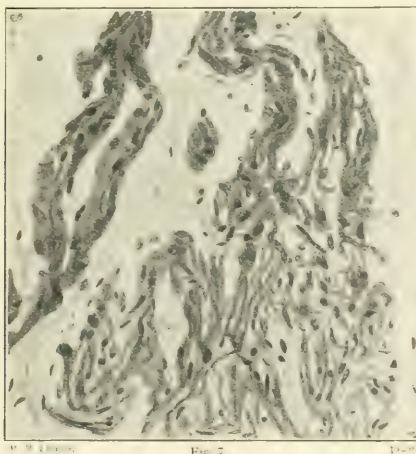


Fig. 7.

Fig. 7. This figure represents the transition fibres between auricle and node. It is a magnification of the portion indicated by the square in Fig. 1 (magnification 300 diam.).

are rich in fine chromatin network. Occasionally transverse striation is seen, but it is not the rule. Their arrangement is very intricate, the fibres interlacing and joining one another without apparent order. At the point of passage from auricle to node (see Fig. 7), they assume a course more nearly parallel, are somewhat plumper, and the fibres of the one become continuous with those of the other. The passage from auricle to node is so gradual that it is quite impossible to say where one begins and the other leaves off. Occasionally it appears as if an auricular fibre divides into two or more smaller node fibres.

To the description of the posterior connection in the *dog* given by Tawara there is little to add. Stress must be laid on the fact that it is always to be demonstrated and maintains the bridge between auricle and the auriculo-ventricular system. The node is usually to be found on the right side, though it may take up a median position, and receives junction fibres at all the points of its circumference. The fibres of the posterior portion of the system do not so constantly assume a parallel course as in the cat and monkey. The plexiform structure is maintained, but becomes more wide-meshed: the fibres then gradually run more parallel, and the transition to auricular fibres takes place imperceptibly. Two or three nodal fibres may unite to form an auricular fibre, a nodal fibre may be inserted obliquely into an auricular fibre, an auricular fibre may end in a plexus of nodal ones, though this is unusual, or, finally, a single nodal fibre may pass into an auricular. As in the cat nodal fibres are rich in nuclei but poor in striation. As the auricle is approached, the nuclei diminish and the striation becomes more evident.

In the *goat* the Purkinje character of the fibres persists until the point is reached where the auriculo-ventricular system and muscle of the auricle unite, and this character is shown by the node itself. In its posterior portion the cells of the node become smaller, and in general arrangement and appearance, though they remain comparatively larger than in the other animals, they assume the character of the nodal fibres already discussed. The nuclei, however, are larger, oval or round, and somewhat more vesicular. The fibres of this portion are also arranged in more parallel fashion, and pass over by gradations into the auricular fibres. In goats the auriculo-nodal union may occur either by the union of several fibres or by the lateral insertion of a node fibre into an auricular. Frequently the transition takes place more gradually by the loss of nodal and the assumption of auricular characteristics (relatively, the auricular fibres are slender and long, and possess few nuclei). In the three goats examined, the node and the junction with auricle were all on the right side of the septum.

A description of this portion of the auriculo-ventricular system is not complete without reference to the nervous structures associated with it. Tawara noted these in sheep. Results exactly like his were found in this series for goats. In the neighbourhood of the node and in the surrounding auricular musculature of goats there are numerous groups of ganglion

cells and a number of large nerve trunks. Besides these, rather thick nerves accompany the branches of the main stem and its two branches, being intimately associated with the Purkinje fibres. Furthermore, in dogs, cats, and rabbits, collections of ganglion cells can almost always be found in the interauricular system close above the transition of auricle to node. Frequently nerve fibres can be found not only in the immediate neighbourhood of node and main stem, but actually accompanying the latter for varying distances. In several cases, also, a nerve trunk was found in the inter-ventricular septum close to the point of division of the main stem of the bundle into its branches, and this nerve trunk also divided into two, right and left. In the monkey no nerves were found in or near the bundle or node, but many were seen in the interauricular system.

Nerves of the kind here described are larger sized trunks, which can be made out plainly with Van Gieson's stain. It lay apart from the purpose which the sections were meant to serve, to employ special methods such as Wilson¹⁵ has employed, and by the employment of which he was able to describe the fine nerve plexuses and fibres, which accompany the muscle fibres of the bundle, and which were previously known to exist in the remaining musculature of the heart.

CONCLUSIONS.

1. The auriculo-nodal connection is constant.
2. The auriculo-nodal junction is subject to considerable variation according to the position occupied by the node. Under different circumstances the fibres uniting auricle and node may join any surface of the latter.
3. The anatomical variations at the auriculo-nodal junction may be explained as due to embryologic variations in the formation of the auriculo-ventricular groove at the membranous septum.
4. Coarse nerve structures are found constantly in the interauricular septum: they are always seen in the auriculo-ventricular system of the goat, frequently in that of the cat, rabbit, and dog, but not in that of the monkey.

BIBLIOGRAPHY.

- ¹ ASCHOFF (L.) for NAGAYO. Ueber den Glykogengehalt des Reitzleitungensystem des Säugetierherzens. *Verhandl. d. deutsch. pathol. Gesel.*, 1908, 150.
- ² BRAEUNIG (K.). Ueber muskulöse Verbindung zwischen Vorkammer und Kammer bei verschiedenen Wirbeltieren. *Archiv f. Anat. u. Physiol.*, 1904, Phys. Abth., Supplement 1.
- FAHR. Ueber die muskuläre Verbindung zwischen Vorhof und Ventrikel (das Hiss'sche Bündel) in normalen Herzen und beim Adams-Stokes'schen Symptomenkomplex. *Virchow's Archiv*, 1907, CLXXXVIII, 562-578.
- ⁴ Gaskell (W. H.). On the Innervation of the Heart, with especial reference to the Heart of the Tortoise. *Journ. of Physiol.*, 1883, iv, 43-128.

- ¹ HIS (W. J.). Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen. Arbeiten aus der medizinischen Klinik, Leipzig, 1893, 14-50.
- ² KEITH and FLACK. The Auriculo-ventricular bundle of the Human Heart. *Lancet*, 1906, II, 359-364.
- ³ KEITH and FLACK. The Form and Nature of the muscular connection between the primary divisions of the Vertebrate Heart. *Journ. of Anat. and Physiol.*, 1907, **XLI**, 172-189.
- ⁴ KENT (A. F. S.). (a) *Proc. Physiol. Soc.*, Nov. 12, 1892; (b) *Researches on the Structure and Function of the Mammalian Heart. Journ. of Physiol.*, 1893, **xiv**, 233-254; (c) *On the Relation of Function to Structure in the Mammalian Heart. St. Thomas's Hospital Reports*, 1893, **N.S.**, **xxi**, 149-161.
- ⁵ KOCH (W.). Ueber die Struktur des oberen Cavatriechters und seine Beziehungen zum Pulsus irregularis perpetuus. *Deutsch. med. Wochenschr.*, 1909, No. 10.
- ⁶ MARCHAND (F.). Ueber eine Geschwulst aus quergestreiften Muskelfasern mit ungewöhnlichem Gehalt an Glykogen, nebst Bemerkungen über das Glykogen in einigen fötalen Geweben. *Virchow's Archiv*, 1885, **c**, 42-66.
- ⁷ MONCKEBERG (J. G.). Untersuchungen über das Atrioventrikulärbündel im menschlichen Herzen. *Gustav Fischer, Jena*, 1908.
- ⁸ PALADINO (G.). Contribuzione all'anatomica istologia e fisiologia del cuore. *Movimento med. chirurg.*, Napoli, 1876 (cited by Bardeleben).
- ⁹ RETZER (R.). Über die muskulöse Verbindung zwischen Vorhof und Ventrikel des Säugetierherzens. *Archiv f. Anat. u. Physiol.*, 1904, *Anat. Abth.*, 1-15.
- ¹⁰ RETZER (R.). Some Results of recent Investigations on the Mammalian Heart. *Anat. Record*, July, 1908, **II**, 149-154.
- ¹¹ TAWARA (S.). Das Reitzleitungssystem des Säugetierherzens. *Gustav Fischer, Jena*, 1906.
- ¹² WILSON (J. G.). The Nerves of the Atrioventricular Bundle. *Proceedings of the Royal Society*, 1909, **Series B**, **LXXXI**, 151-164.

FURTHER STUDIES IN THE PHYSIOLOGY OF HEART-BLOCK IN MAMMALS. CHRONIC AURICULO-VENTRICULAR HEART- BLOCK IN THE DOG.

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and of the University of Wisconsin.)

OUTLINE.

Introduction.

Methods—

Description of operation.

Methods of study.

Results—

General account of experiments.

Cases with complete and, for the most part, permanent block.

The proof that the block was complete.

Usual rate of auricles and ventricles.

Some conditions affecting the rate of the ventricles in complete block.

Heart irregularities—

I. Aperiodic irregularities.

(a) *Variability of ventricular cycles.*

(b) *Ventricular extrasystoles.*

II. Periodic irregularities.

(a) *In association with Cheyne-Stokes respiration.*

(1) *The more marked grades, and the associated symptoms in man and dog.*

(2) *The less marked types.*

(3) *Periodicity of the auricles dependent upon ventricular activity.*

(4) *Mechanism of the several types.*

(5) *Irregularity associated with sighing respiration.*

*(b) Group beating of the ventricles.**Symptoms associated with group beating of the ventricles.**General symptoms of the cases of complete heart-block.**Mode of death, and autopsy findings in general.**Histological findings.**Relation of respiratory to ventricular rhythm.**Final experiment on Dog No. 13.**Relatively complete heart-block with recovery.**Summary.**Conclusions.**Protocols of experiments.*

INTRODUCTION.

THE experiments on heart-block in mammals which have hitherto been reported, while indicating clearly the identity of Stokes-Adams disease in man and auriculo-ventricular heart-block in the dog, have left with controversial or unsatisfactory explanations many of the signs and symptoms of the disease in man². While conversing with Dr. William H. Welch on this subject, the conception arose that if chronic heart-block could be produced experimentally in some mammal, and if in this way the clinical picture of Stokes-Adams disease could be duplicated, we would then be in a position to investigate the phenomena of that disease more exactly than is possible clinically. At the same time it was hoped that such experiments might throw more light upon certain questions concerning the physiology of the heart beat.

The term "heart-block" (it would be better to specify auriculo-ventricular heart-block) is now generally employed to designate a condition caused by partial or complete interference with the normal sequence of the auricles and ventricles. The interference may manifest itself merely as a pause, longer than usual, between the contractions of the auricles and ventricles, or as occasional, regular, or total failure of the ventricles to respond to auricular contractions. There are many factors which may interfere with the normal auriculo-ventricular rhythm. This paper, however, deals only with functional insufficiency caused by mechanical interference with the transmission of the excitation wave from auricles to ventricles.

Recent experiments have demonstrated beyond peradventure that heart-block is the invariable result of cutting, crushing, or injuring in some other way only that region of the auriculo-ventricular junction through which courses the auriculo-ventricular bundle of His. To state the facts in another way, the auriculo-ventricular bundle constitutes the only

functional connection between the auricles and ventricles of the mammalian heart*. It should furthermore be added that, since animal experiments have demonstrated the functional importance of the auriculo-ventricular bundle, it has been found that disease of this minute structure, and of it alone, is the cause of heart-block, properly so called, in man†.

There is, we believe, but one possible objection to the sweeping assertion that the auriculo-ventricular bundle constitutes the only functional connection between the auricles and ventricles of the mammalian heart. It is not unreasonable to maintain that other connections exist which, under ordinary circumstances, are dormant, and that, in the course of the few hours occupied by heart-block experiments as hitherto performed, they do not have sufficient time to assume vicariously the functions which normally are performed by the auriculo-ventricular bundle. This objection seems to be met by those instances in man in which a lesion, more or less accurately limited to the region of the auriculo-ventricular bundle, has undoubtedly served to block permanently the passage of the excitation wave through the auriculo-ventricular junction‡. Certainly, in such instances, sufficient time has elapsed for the assumption of the functions of the auriculo-ventricular bundle by other hypothetical structures. Nevertheless, clinical observations, even when confirmed by post mortem findings, do not carry with them the conviction of a clean cut experiment. The possibility is always present that tissues, other than those found diseased, may be the seat of pathological processes which, however, have escaped detection.

Furthermore, the animal experiments heretofore reported do not positively answer the question—Is the conducting tissue of the auriculo-ventricular bundle muscular or nervous? It cannot be denied that their evidence supports the former view. There seem to be strands of nervous tissue stretching from the auricles into the ventricles in many parts of the auriculo-ventricular junction, whereas the auriculo-ventricular bundle constitutes the only muscular bridge: destruction of this connection alone produces heart-block. Nevertheless, it is justifiable to maintain that the function of conducting the cardiac excitation wave resides, not in all nervous structures, but rather only in those nervous elements which are in the

* All laboratories with but a single exception are in accord with this conclusion. Paukull¹⁴, working in Kronecker's laboratory, states that ligatures laid around the auriculo-ventricular bundle do not cause block, while ligatures in other places may. The accumulated evidence of all other laboratories forces us to conclude that there was some source of error in Paukull's observations.

† Our facilities for referring to the clinical literature are very limited. A recent review of the subject by Lewis will be found in *B.M.J.*, Dec. 16th, 1903.

‡ Heineke, Müller, and v. Hösslin describe a case of disturbed conductivity in man without the Stokes-Adams syndrome, in which the bundle was found completely obliterated. Nevertheless, they state that the ventricles frequently contracted with the auricles, and consequently believe they are justified in assuming that under certain circumstances, together with long duration of the affection, other routes for the conduction of the cardiac impulse may be developed. Lewis, however, states that these authors are not justified in drawing this conclusion because their last observations were made six weeks before their patient's death.

closest relation with the musculature of the heart. Such elements would, therefore, probably find their way across the auriculo-ventricular junction with the musculature of the auriculo-ventricular bundle.

Finally, clinical observations seem to indicate that Stokes-Adams disease with complete dissociation of the beats of the auricles and ventricles may be recovered from. For instance, a case with complete auriculo-ventricular heart-block giving a syphilitic history recovered completely under treatment with iodides². Such observations suggest that the auriculo-ventricular bundle, or the special conducting tissue in it, if such there be, may regenerate after complete severance of its continuity. The practical importance of determining whether or not such is the case is obvious.

These then are some of the questions which it was hoped might be elucidated by a study of animals surviving experimental interference with the function of the auriculo-ventricular bundle.

Consequently, in February, 1906, a series of experiments upon this subject was begun, in collaboration with E. K. Cullen. A preliminary report of this series, consisting in all of seven experiments, was made before the Johns Hopkins Medical Society on 23rd April, 1906³. These experiments were interrupted by a change of residence by one of us, when, owing to lack of necessary apparatus, they could not be resumed until March, 1907. At this time, in collaboration with J. R. Blackman*, the research was carried to a state of more or less satisfactory completion⁴.

METHODS.

Description of the operation.—All of the experiments were performed upon dogs anæsthetised with morphine and ether. The operation for the production of heart-block was varied from time to time. In general, however, the technique was as follows :—After having inserted a tracheal cannula, an incision, 6 to 10 cm. long, was made on the right side close to the sternum, parallel to, and in the second or third intercostal space through the skin, and down to the intercostal muscles. Through this incision pieces of the second and third, or third and fourth ribs about 6 cm. long were excised together with the attached intercostal muscles and parietal pleura. After opening the pleural space artificial respiration was begun. In the first seven experiments the usual intermittent inflation of the lungs was employed for this purpose ; in the remainder, a modification of Brauer's method, the positive pressure being exerted upon the lungs through the tracheal cannula. The pericardium was then incised and the cut edges stitched to the edges of the wound

* A preliminary report⁴ of the results of all experiments was made shortly after their completion. This final report has been delayed in order that the histological findings might be available.

in the chest wall. The connective tissue at the root of the aorta was grasped in a long strong artery clamp, and, by means of traction exerted through the clamp, the heart was drawn well up into the wound in the chest wall.

Heart-block was then produced in one of three ways :—

(1) With a hypodermic syringe, the needle of which was so guarded that the point could be inserted no further than the desired depth, an attempt was made to inject a solution of iodine in alcohol into the auriculo-ventricular bundle. The needle was inserted in different positions, and the solution injected until heart-block resulted. Attention should be called to the fact that heart-block obtained by the use of this uncertain method is not necessarily due to the injection of the solution directly into the bundle ; fluid forced into the heart tissue close to that structure might, through compression, interfere with its function. A block so produced might disappear with the absorption of the fluid, or it might become more complete through the spread of an inflammatory process from the place primarily injured. Indeed, iodine was employed in these experiments in the hope that it would set up a chronic inflammation which would gradually spread to the surrounding tissues. In this hope we were, however, disappointed.

In the remaining experiments the auriculo-ventricular bundle was crushed in the heart clamp devised by one of us for the purpose of producing heart-block acutely in mammals⁵.

(2) At first the clamp was applied to the heart in the manner that has been described in earlier publications ; one arm was inserted into the left ventricle through the root of the aorta. This was found to be a rather difficult procedure, the small size of the opening in the chest wall through which the clamp had to be manipulated greatly hampering its proper adjustment.

(3) In the present experiments we found it easier to insert the L-shaped part of the clamp into the septum of the ventricles below the bundle by pushing it through the wall of the right auricle into the right ventricle. The position at which the point of the clamp should be inserted into the interventricular septum can easily be determined by momentarily grasping the upper edge of the septum between the thumb, invaginating the right auricle before it, and the index finger invaginating the left auricle before it. For these experiments the barb was removed from the point of the L-shaped arm so as to facilitate its withdrawal after block had been produced. In order to prevent its slipping from place before it was desired to withdraw it from the heart it was simply necessary to constantly exert pressure upon it in the proper direction. Then, when it was found that tightening the clamp blocked the impulse on its way from auricles to ventricles, the tissue in the grasp of the clamp was thoroughly crushed, and the clamp removed. The heart was then watched for some minutes, and when we were reasonably certain that complete heart-block had been produced, the wounds were closed : first, the pericardium, with a continuous suture ; then the chest wall, with interrupted sutures, care being taken to obviate pneumothorax ;

and finally, after having assured ourselves that the respirations were efficient, the tracheal wound. The operations were performed aseptically; in only one case did the chest wound break down. The accidents encountered can best be considered in connection with the histories of the several cases.

Methods of study.—Usually, during the ten days immediately following the operation, that is to say, before the bandages were removed, the arterial pulse rate and rhythm were determined by palpation. When, in any case, the pulse became irregular to such a degree as to suggest that something of interest might possibly be determined by a more careful study of it, tracings upon a Hürthle kymograph were made of the pulse in the leg, using as a sphygmograph the sphygmomanometer of the author. In lieu of cardiograms this method proved to be very satisfactory, and it possessed the further advantage of being easy of application. After the removal of the bandages the study was continued by the aid of cardiograms. With the exceptions to be noted below, these were made daily as a matter of routine. Upon the appearance of anything unusual more careful and lengthier tracings were made. During July and August, and the first half of September, 1907, on account of the enforced absence of the authors, the animals were watched by an attendant who counted the pulse daily and noted unusual symptoms. From September until February, 1908, owing to the press of other work, it was found possible to make tracings only occasionally, although a close watch was kept over the animals.

In order to facilitate the making of tracings, the animals were trained to lie quietly, usually with the operated side downwards. Through a space between two adjoining tables the receiving instrument was applied to that part of the chest wall from which the ribs had been removed. At first, Marey's cardiograph was employed as the receiving instrument; later, a funnel. In the latter case, the chest was shaved and the edges of the funnel vaselined. The records were made in the usual way by means of air transmission. The curves obtained show the movements of the ventricles and auricles, or, better, those movements of the auricles which are not obscured by the stronger movements of the ventricles. The time was recorded in fifths of seconds. In a vast majority of the records it was then a simple matter to determine the rate of the auricles by measurement of the tracings, after allowing for the obscured contractions. Occasionally, however, the auricles were so irregular that this method of estimating their rate proved valueless. As satisfactory records of the venous pulsations could not be obtained, it was then impossible to determine the auricular rate accurately.

Special experiments requiring special technique were performed from time to time. Accounts of the methods used in such cases will be found in their proper places.

RESULTS.

GENERAL ACCOUNT OF EXPERIMENTS.

Thirteen attempts were made to produce auriculo-ventricular heart-block in the surviving dog. Four of the dogs died on the table, three (Nos. 5, 9, and 10) of hæmorrhage through the puncture made in the heart by the clamp; (No. 6) of some unknown cause. No. 1 died a few hours after the operation, probably of iodine poisoning, while No. 2 died two hours after the operation of hæmorrhage through the puncture in the heart.

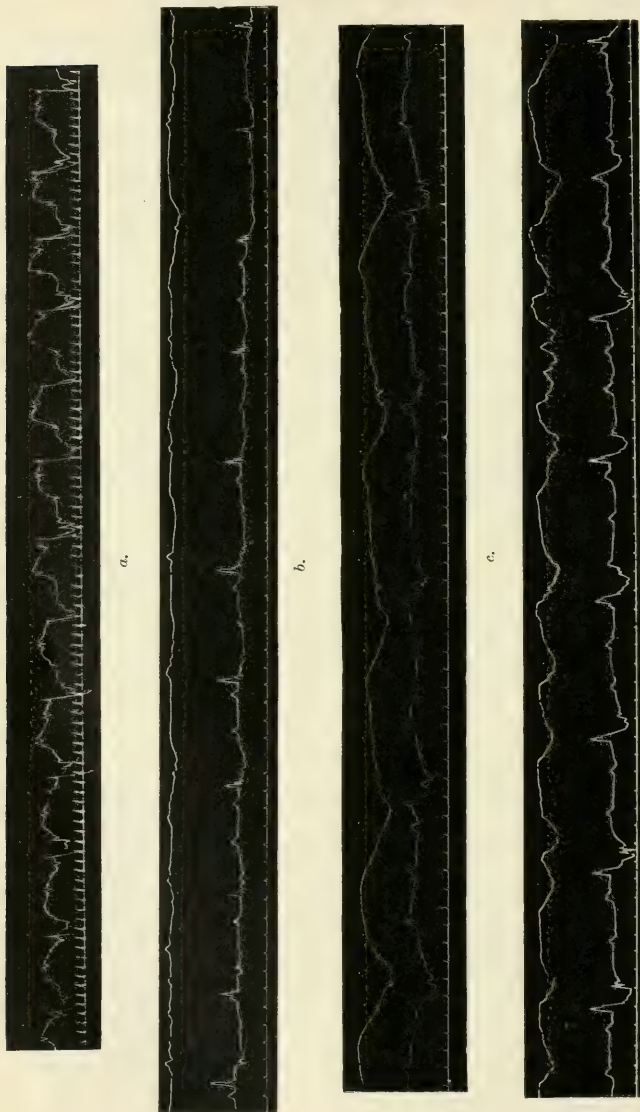
The remaining animals (Nos. 3, 4, 7, 8, 11, 12, and 13) survived the operation long enough to permit of a study of its consequences. By way of introduction, the results obtained in these cases may be summarised as follows:—One animal (No. 3) had relatively complete auriculo-ventricular block, from which it gradually recovered in the course of 26 days. No. 4 had, immediately after the operation, a very slight grade of block which disappeared completely within 48 hours. Dogs No. 7, 8, 11, 12, and 13 survived the operation from 6 to 343 days. All, possibly with one exception (No. 8), had complete and permanent auriculo-ventricular heart-block. No two of the cases were, however, entirely alike, although some features were common to all, or to most, of them.

CASES WITH COMPLETE AND, FOR THE MOST PART, PERMANENT AURICULO-VENTRICULAR HEART-BLOCK.

We shall consider first the cases in which the block was complete and permanent, together with the doubtful case.

The proof that the block was complete.

It is justifiable to assume that the ventricles are beating independently of the auricles when the cardiograms show two series of waves each more or less regular in rhythm, but without any constant relation the one to the other⁶. Fig. 1 shows small sections of cardiogram chosen at random from each of four cases—*a* from case 7; *b* from case 8; *c* from case 12; and *d* from case 13. There should be no difficulty in recognising by inspection of this figure that in all cases the heart-block was complete. At other times, however, it occasionally happens that, through short stretches of record, one auricular wave—the second or the third of each ventricular cycle—bears a more or less constant relation to the corresponding ventricular waves. It cannot be positively affirmed that at such times the block was complete; but since such stretches were almost invariably preceded and followed by tracings evidently made by a heart in



* Fig. 1 *a-d*. Tracings from (*a*) Dog No. 7 (1st April, 1906); (*b*) Dog No. 8 (3rd May, 1907); (*c*) Dog No. 12 (21st September, 1907); (*d*) Dog No. 13 (1st May, 1907) showing complete block.

* In any figure consisting of two traces, unless otherwise stated, the upper is respiratory (down strokes marking inspiration), the lower cardiac. The time is marked in fifths of seconds, unless otherwise stated.

complete block, and, furthermore, since they appeared so infrequently, we believe the conclusion to be justifiable that the block was complete at all times even while these tracings were being inscribed, and that the 2:1 or 3:1 sequence seen in these places was entirely accidental. We have frequently obtained in the course of previous experiments on heart-block similar tracings in which the block appeared to be partial at times when it undoubtedly was complete.

In the case of Dog No. 8, however, the times when there was some doubt as to the completeness of the block recurred so frequently and occasionally lasted so long as to force us to conclude that at least in one stage of this animal's history the block was relatively complete: indeed, that at times it was partial (see Fig. 2). The period in which the block may not have been complete extended from about the fifteenth to the forty-second day.

These observations are in complete accord with the histological examination which shows that the auriculo-ventricular bundle had been almost but not completely crushed across.

The question then arises—Why was the block complete in the earlier and later stages of this animal's history, while at other times it was partial? This difficulty is probably to be explained away as follows. The portions of the bundle that had escaped complete destruction were injured to such an extent at the operation as to have been rendered functionally insufficient. Such insufficiency was maintained subsequently and until about the fifteenth day by the transudation of blood and lymph associated with the injury. With the subsidence of the inflammation the part of the bundle undestroyed sufficed to occasionally conduct impulses. Later, however, after the forty-second day, the functional capacity of the remaining part of the bundle was again diminished, probably through its inclusion in a contracting scar.

Dog No. 11 lived but six days, and consequently we have only sphygmograms, coupled with certain inferences, as evidence upon which to base our opinion. We feel justified, however, in concluding from such meagre evidence that the block in this case, too, was complete. The evidence consists of (a) the slow pulse (see Table No. 1); (b) pulsations seen at times in the neck (probably in the veins), which were more frequent than the arterial pulse and seemingly quite independent of them; and (c) stoppage of the ventricles with development of rhythm (see p. 199).

Usual rate of auricles and ventricles.

Table No. 1 shows in columns 3 and 7 what we may term the usual rate of auricles and ventricles of the cases of complete heart-block. These figures were not obtained by striking an average of all estimations made, since that method would have included many abnormal values. It was



Fig. 2. Showing what is probably a partial block, the rhythm being for the most part 2 : 1, with an occasional 3 : 1 cycle.
Dog No. 8 (8th April, 1907).



Fig. 3. Showing irregular variations in the duration of the ventricular cycles. Dog No. 8 (3rd April, 1907).
The block is probably complete.

TABLE I. Showing the auricular and ventricular rates in dogs with complete auriculo-ventricular block.

| No. of Dog. | Weight at end In K. | VENTRICULAR RATE. | | | | AURICULAR RATE. | | | | Duration of Life (Days.) | Manner of Death. | REMARKS. | |
|-------------|---------------------|-------------------------|-------|------|--------------------------------|-------------------------|----------------|------|---------------------------|--------------------------|------------------|--------------|------------------------------------|
| | | Under usual Conditions. | | | Max. under unusual Conditions. | Under usual Conditions. | | | Under unusual Conditions. | | | | |
| | | Average (approx.) | Max. | Min. | | Average (approx.) | Max. | Min. | Max. | | | | Min. |
| | | | | | | | | | | | | | |
| 7 | 7.7 | 40 | 59.0 | 34.7 | 70.0 | 100 | 116.8 | 79.8 | 137.7 | 63.4 | 28 | Sudden | Cheyne-Stokes type of periodicity. |
| 8 | 9.2 | 50 | 74(?) | 34.0 | 105.0 | 145 | 180.0 | 97.0 | 236.2 | | 92 | Sudden | Syncopeal attacks. |
| 11 | 7 | 35 | 48.0 | 28.0 | — | | Not determined | | | | 6 | Pericarditis | Epileptiform seizures. |
| 12 | 23.9 | 45 | 53.5 | 31.5 | [27 (min.)] | 150 | 176.2 | 99.7 | 202.5(?) | 42.7 | 320 | Sudden | Syncopeal attacks. |
| 13 | 17.5 | 39 | 46.8 | 30.0 | 71.4 | 120 | 154.0 | 75.0 | 165.0 | 37.5 | 343 | Killed | No symptoms. |
| Averages | | 41.8 | 56.3 | 31.6 | 82.1 | 129 | 156.7 | 87.9 | 185.3 | 46.2 | | | |

Chayne-Stokes type of periodicity.

Syncope attacks.

Epileptiform seizures.

Syncope attacks.

No symptoms.

thought better to peruse the columns of figures in the protocols, and then to set down the figures about which the normal values seemed to range. This figure, it will be seen, is different in each case. The ventricular rate was slowest in the case of Dog No. 11 (35 per minute). It is possible that the acute purulent pericarditis from which the animal was suffering may have accounted in part for the slow rate of beat. The ventricular rate was fastest in the case of Dog No. 8 (50 per minute).

For these differences in ventricular rate we have been unable to account. The table shows that they are not wholly due to differences in body weight. If weight be a factor, the relation is obscured by other factors, such, possibly, as nervous state, temperature (season of year when observations were made), age, etc.

Under what we may term normal circumstances the range of ventricular rate in any given case, excepting No. 8, is not very great. It does not, with the exception mentioned, much exceed 20 beats per minute, the average range, including all cases, being somewhat less than 25 per minute.

The average of the usual auricular rate is 129 beats per minute; the ratio of the usual ventricular to auricular rate is, therefore, 3.09. We place here for comparison a table (No. II) showing the A-V ratio in cases of heart-block

TABLE II. Showing the A-V ratio in acute heart-block in the dog and in two cases of chronic heart-block in man.*

| SUBJECT. | RATE PER MINUTE OF | | A V RATIO. | REMARKS. |
|----------------|--------------------|-------|------------|-----------------------------|
| | V. | A. | | |
| Dog | 54.1 | 162.1 | 3.05 | Average of many estimations |
| Man. Case 1 .. | 22.4 | 79.6 | 3.55 | Maximum ratio. |
| " " 1 .. | 31.0 | 84.6 | 2.73 | Minimum ratio. |
| " " II .. | 31.7 | 89.3 | 2.82 | Single observation. |

* Modified somewhat from a table published by one of the authors².

in the dog determined within a few hours after its production, and also the A-V ratio in two cases of chronic heart-block in man which we have had the opportunity of studying. It is interesting to note the similarity of the ratios under different conditions in the case of one and the same species as well as in widely separated species. Since the A-V ratio is probably a measure of the relative rhythmicity of the *primum movens* of the heart and the ventricles, the values here given suggest the existence of some cause, possibly teleological, for its constancy, despite decided differences in rate.

The usual auricular rate, average 129, is somewhat higher than the heart rate in normal dogs, as given by Volkmann, 100 to 120 per minute. This is not surprising when it is recalled that in heart-block, with its slow ventricular rate, the circulation must be sluggish, and the vagus tone

consequently low. Nevertheless it is interesting to note that even under usual circumstances the auricular rate may be slower in heart-block than Volkmann's normal minimum. Thus, in each of our cases the minimum rate fell at times below 100.

Compared, therefore, with the absolute range of auricular rate in heart-block, 68.8, that of the ventricles, approximately 20, is very small, although the ratio of minimum to maximum rates is practically the same, being about 0.56 in the case of both the auricles and ventricles.

Some conditions affecting the ventricular rate during typical heart-block.

Although constancy of the ventricular rate from day to day is a striking feature of cases of heart-block in the dog, and we might add, in man, too, nevertheless under unusual conditions the range of ventricular rate may be a wide one, as may be seen in the table. Some of the factors influencing the ventricular rate may be briefly referred to here.

(a) *Nervous states*, such as are seen while an animal is being trained to lie still, so that cardiograms may be made, markedly increase the ventricular rate. Thus, the ventricular rate in the case of Dog No. 7 was 70 per minute the first time tracings were made.

(b) In some instances the *afternoon* rates are in general faster than the *morning* rates. This may have been either a temperature effect or merely a manifestation of diurnal variations.

(c) The *muscular exercise* of running, together with the accompanying mental exhilaration, likewise increases the ventricular rate. Table III shows this effect clearly. Conversely, it would appear that

TABLE III. Showing the results of a few typical experiments testing the effect of exercise on the rates of the auricles and ventricles in complete block.

| NO. OF DOG. | DATE. | IMMEDIATELY BEFORE EXERCISE. | | IMMEDIATELY AFTER EXERCISE. | |
|-------------|--------|------------------------------|-----------------|-----------------------------|-----------------|
| | | A RATE PER MIN. | V RATE PER MIN. | A RATE PER MIN. | V RATE PER MIN. |
| 8 | June 5 | 135.0 | 49.5 | 146.2 | 55.5 |
| 8 | " 6 | 157.5 | 54.0 | 157.5 | 57.7 |
| 12 | " 6 | 142.5 | 46.5 | 172.5 | 62.2 |

the ventricular rate is diminished somewhat when, under ordinary conditions, the animal rests quietly upon the table. This is, however, difficult to demonstrate clearly for the reason that the animal usually becomes restive after a time.

(d) The ventricular rate is notably fast in animals under *ether*. For example, two of the dogs, Nos. 8 and 13, were anaesthetised on the

eightieth and seventy-fifth days respectively. In the case of the former, the rate under ether was 105 compared with 57 under normal circumstances on the preceding day, and 67.5 on the same day but subsequent to anæsthetisation; while in the case of Dog No. 13 the ventricular rate under ether during an operation was 71.4, whereas under the influence of morphine immediately before the administration of the ether it was 39, and on the day following, 42.7 beats per minute.

(e) The effect of *morphine* is illustrated in the preceding data; it was studied more carefully, however, upon another occasion. The ventricular rate immediately before a hypodermic injection of $1\frac{1}{2}$ gr. of morphine was 37.5, it became 33 when the animal was fully under the influence of the drug, and with the administration of ether the rate increased to 49.5 beats per minute.

(f) The effect of *digitalin* upon the heart was tested in the case of Dog No. 12. In the course of 44 minutes 4.5 cc. of a 1 per cent. solution of the crystalline alkaloid (Merck's) were injected intramuscularly. This dose was without obvious effect, although subsequently an abscess developed at the seat of injection. The effect of a still larger dose was not tried through fear of deleterious action.

(g) The effect of *atropin* was not tested on animals with complete block. It is, however, well seen in the case of the dog with partial block, to be considered later (p. 215).

The auricular rate, in the conditions mentioned above, is usually affected as is the whole heart when normal. This is not, however, the case with the ventricular rate. The respective rates of the auricles and ventricles may, therefore, suffer contrary variations. An interesting instance of this is given on p. 207.

Heart irregularities.

For convenience of description the irregularities of heart beat we have met with may be divided into two groups, namely, (1) aperiodic irregularities; and (2) periodic irregularities.

(1) *Aperiodic irregularities* were comparatively rare. Indeed, one of the remarkable features of these cases is that, despite the profound change in the way in which the heart performs its work, its action for the most part is perfectly regular in that successive ventricular cycles recorded under constant conditions are of approximately the same duration.

(a) Occasionally, however, in the case of two of the dogs, Nos. 8 and 12, and early in their histories, considerable *variability of the ventricular rate* was seen. Thus, in the case of Dog No. 8, on 1st and 3rd April, the duration of the cycles varied irregularly in one place between 1.2 and 0.84 sec. (Fig. 3). In the notes made on the twenty-fifth day of Dog No. 12 it is recorded

that there were scattered irregularly and singly in the midst of cycles of an average duration of 1.45 sec., ventricular cycles of about 2 sec. duration. These irregularities were without apparent cause. The possibility of an incomplete block must, however, be entertained in the case of Dog No. 8.

(b) *Ventricular extrasystoles* were seen upon one occasion only, namely, in the course of an experiment testing the action of digitalin upon the heart in the case of Dog No. 12. Only three were recorded. The extra cycles were always a little longer than the normal periods, but they were never compensatory.

(II) *Periodic irregularities*.—Under this caption two exceedingly interesting and, in most respects, characteristic irregularities will be described.

(a) *Periodic variations in the rate of the auricles, sometimes associated with periodic variations in the rate of the ventricles, and with Cheyne-Stokes respiration*.

This type of irregularity was met with in all of the animals that lived long enough to allow of careful study (all excepting Dog No. 11), although it varied greatly in the different cases, and even in the same animal from time to time.

(1) It will be convenient to describe first what we believe to be the *most marked grade* or better, perhaps, the most perfectly developed instance of this type of irregularity. On several days early in the month of April, but especially on the fourth day of that month, the following phenomenon was observed in the case of Dog No. 7 (Fig. 4):—

The respirations were of the Cheyne-Stokes type, though there was never at any time complete apnœa; the respirations periodically became slow and shallow. With the onset of the period of quiet respirations the successive auricular cycles lengthen, and reach their maximum duration often in the course of 2, 3, or 4 cycles. The increase in extreme cases may be from a cycle lasting 0.4 sec. to one lasting more than 1.6 sec.. At this time the ventricular cycles are short, but toward the end of the period of quiet breathing they begin to lengthen at such a rate that with the second or third respiration of the dyspnœic period they have attained their maximum duration. In extreme instances the duration of the ventricular cycle has increased from 1.6 sec., or even less, to 4.4 sec.. Briefly, slowing of the ventricular rate occurs more or less synchronously with acceleration of the auricular and respiratory rates.

In cases of heart-block in man a syndrome has been observed similar in every respect to the one just described: "At one time the patient developed a mild form of Cheyne-Stokes respiration. At this time typical (syncopal) attacks, with marked slowing of the ventricles, occurred with great regularity. The slowing of the ventricular rate usually began, say, in the period of dyspnœa just at the time when in other conditions associated with Cheyne-Stokes respiration of the cardio-vascular type,

the heart rate begins to increase¹⁹. The auricles show this increase in rate, but . . . the ventricular rate diminishes when the auricular rate begins to increase." "The subjective symptoms of these attacks were usually very mild; in them the patient never actually lost consciousness, although he undoubtedly would have fallen had he been up and about. The patient called them 'dizzy' spells."²

In this connection it should be added that, excepting slight restlessness during the period of dyspnoea (period of slow ventricular beats), there were no obvious symptoms associated with the phenomenon in the case of our Dog No. 7.

It has been stated that less perfectly developed types of periodicity have also been observed.

(2) Thus, in the case of Dog No. 7 we have seen *Cheyne-Stokes respiration with marked periodicity of the auricles*, and only the slightest or no periodicity of the ventricles; also marked periodicity of the auricles only, at times when the respiratory rhythm was quite regular. Neither Dog No. 12 nor 13 had at any time distinct Cheyne-Stokes respiration. Nevertheless, these animals, particularly the latter, exhibited at times marked variations in the rate of the auricles (Fig. 5). Often in these case the variations in rate did not recur with perfect rhythmicity, and again the auricles were often slow over long periods of time. Upon one occasion only was it noted that the ventricular rate increased during the periods of slow auricular rate.

(3) *Periodicity of the auricles dependent upon ventricular activity.*—Occasionally, in the case of Dogs Nos. 12 and 13, while the type of irregularity just noted was in evidence, just one auricular wave was inscribed in each ventricular cycle during the period of auricular retardation. Not infrequently during comparatively long periods of time this single auricular wave per ventricular cycle was located close to the ventricular wave that terminated the cycle (Fig. 6). In this way the effect is produced of a 1:1 auriculo-ventricular rhythm with long and variable As-Vs periods. We are of the opinion, however, that we are dealing here, not with a 1:1 rhythm, but rather with a marked degree of another type of periodic irregularity, namely, a lengthening of the auricular cycles following each contraction of the ventricles.

Upon several occasions during the period of slow auricular rate no auricular waves at all were visible over comparatively long stretches of record (Fig. 7). Such complete disappearance of auricular waves may have been apparent only. There may have been just one auricular wave in each ventricular cycle, occurring during ventricular activity, and obscured thereby.

In the less extreme types it may be seen that the first auricular cycle following a ventricular contraction is long, but that the successive auricular cycles shorten until the ventricles again contract (Fig. 1c and d).

This type of irregularity in all of its variations was frequently met with in the case of Dog No. 13.

It would appear that we probably have to do here with rhythmical variations of vagal tone, which increases with each arterial pulse only to diminish again during the interval between pulses. The fact that but one auricular wave is seen in each ventricular cycle and close to its termination might be explained by premising the existence of a continued high grade of vagal tone (see p. 208), which is diminished sufficiently during each ventricular cycle to permit of but a single auricular beat.

The factors determining the appearance of these types of periodic auricular irregularity, at least in the case of Dogs Nos. 12 and 13, seem to be (a) long continued heart-block; and (b) complete repose. Thus, in the case of Dog No. 12, the advanced type of this irregularity was first observed in an experiment performed at the close of its third month, for the purpose of determining the action of digitalis upon the heart beat. We are sure that it was not a digitalis effect. It resulted from the prolonged repose necessitated by the experiment. That such is the case is indicated by the fact that on the next day the irregularity was again observed, but only after the animal had become composed by long rest in the position to which he had been trained to facilitate the making of observations.

In the case of Dog No. 13, this type of periodicity was first noted on the forty-second day, but thereafter was met with infrequently and in a very mild form until after the operation on the vagus nerve on the seventy-fifth day. From that time until the animal's death the periodicity was seen in almost every tracing.

It is interesting to note that in the case of Dog No. 13, at least, when periodic variations in the duration of auricular cycles were evident, the ventricular rate was usually relatively slow. For purposes of illustration we refer to the records of 21st September. Many tracings were made on this day. At first the periodicity of the auricles, although present, was not marked; the rates of the auricles and ventricles were, respectively, 102.7 (?) and 39. Later the periodicity was marked; in the 8 sec. period used for the estimation, the auricular rate, as well as it could be determined, was 37.5, the same as the coincident ventricular rate.

(4) Nothing could be determined with regard to the *mechanism of these several types of periodic irregularity*. If, however, in the case of the extreme form (Cheyne-Stokes respiration with retardation of the ventricles and acceleration of the auricles during the dyspnoëic period), we may be permitted to assume that we have to do with a stimulus that acts upon that part of the respiratory centre stimulation of which stops the respirations, then, since the vagus has but little influence upon the ventricles, the phenomenon might be explained as

being due to rhythmical variations in the intensity of stimulation of all of the medullary centres. Stimulation of these centres, upon the basis of the assumption made above, would slow the respirations and the auricles (through the vagi) while accelerating the ventricles (through the accelerators).

When the stimulus does not affect the respiratory centre, but only the vagus and accelerator centres, the Cheyne-Stokes respiration falls away, while the rest of the phenomenon continues. And finally, when the stimulus in addition fails to act upon the accelerator centre, rhythmical slowing of the auricles alone may persist, or there may even be slight synchronous slowing of the ventricles.

In this connection attention should be called to the fact that the degree of variation of the auricular rate may be much greater than that of the ventricles. Indeed, the slowest ventricular rate recorded in the whole series of experiments was 30, whereas we have seen that in comparatively long periods of time there may be no visible auricular waves. Assuming that the variations in the auricular rate are the result of vagus action, it then follows that vagus impulses of sufficient intensity to completely (?) inhibit the auricles can at most reduce the ventricular rate from a median figure of about 42 to 30. In other words, vagus action in heart-block is much more intense upon the auricles than upon the ventricles.

(5) *Irregularity associated with sighing respiration.*—We wish to record in this place another irregularity which, though not rhythmical, is undoubtedly determined by the same factors upon which depend the rhythmical irregularities noted above. This irregularity, which was associated with a sighing respiration, we have observed but once in the course of our experiments.

Upon a deep sighing respiration, in the case of Dog No. 12, there supervened a period of complete apnoea lasting 24.4 sec. (Fig. 8). The ventricular cycles preceding the sigh lasted, on an average, 2.2 sec.. Immediately after the ventricular period fell to 1.4 sec., but gradually the duration increased until with the eleventh cycle it became practically constant, when the period was 2.46 sec.. Before the sigh, about four auricular waves were visible in each ventricular cycle. Immediately after the auricular rate was very slow, but gradually increased; only one auricular wave was visible in the first three ventricular cycles, one each in the fourth, fifth, and sixth cycles; the auricular rate then gradually increasing until four or five were visible in the thirteenth ventricular cycle. The apnoeic period terminated in the twelfth cycle. In other words, a sighing respiration was followed by a long period of apnoea during which there was marked slowing of the auricles and acceleration of the ventricles. The phenomenon, it will be seen, is identical with that observed in association with Cheyne-Stokes respiration.

(b) *Group beating of the ventricles.*—The other type of arrhythmia observed in these cases consisted of periodic, although somewhat irregular, acceleration of the ventricles. This phenomenon was seen in Dogs Nos. 8, 11, and 12, but an opportunity for studying it carefully offered itself only in the case of Dog No. 12. We shall, therefore, describe in detail first what was seen in this case, and then attempt to correlate with it the similar events seen in the other instances.

On the 3rd of May (that is, the fortieth day), while tending the animals, the attendant, in the course of ten minutes, twice observed that Dog No. 12 almost toppled over without any apparent cause. Tracings were immediately made and they revealed the following interesting irregularities.

In one of the first tracings made groups of from two to five rapid ventricular contractions are separated from one another by long ventricular cycles (Fig. 9). The duration of the longest of such long cycles on this tracing is 2.8 sec., twice that of the average cycle of typical heart-block. The block, at least in the long cycles, is obviously complete; the auricular rate is slow at the beginning of the long cycles, but increases toward their close.

In the very next tracing made (the same day and shortly after the above) the groups of rapid ventricular contractions are much longer; thus, 63 beats at the rate of 180 per minute appear at the opening of the tracing. Series of much greater duration were, however, recorded. For example, during one revolution of the paper over 230 rapid ventricular beats had been recorded when the end of the paper was reached. The beats of a series are not perfectly regular in rhythm. Each series is terminated by stoppage of the ventricles followed by what seems to be a tendency to a gradual resumption of the ventricular rate which is characteristic of heart-block (Figs. 10 and 11). Thus, in one instance, the duration of the successive ventricular cycles in fifths of seconds is—24, 21, 7, 15, 10, 8, 7, when the ventricles abruptly begin to beat rapidly again. Here it is impossible to determine the relation of auricular to ventricular waves, but just previously, while the ventricles are developing their rhythm, it can be seen that they are beating independently of the auricles, whose rate of beat is very rapid. Many records of this irregularity were made on this day.

On the next day (4th May) group beating of the ventricles was encountered rather infrequently. Thus, it was not met with during one revolution of a long record on the Hürthle kymograph. This record showed the block to be typically complete, the auricular rate being 142.5, the ventricular rate 46.5 beats per minute. While the paper was making its second revolution the irregularity reappeared. The record of typical block is here followed by a series of rapid ventricular contractions, the rate of the ventricles being 141 per minute. The relation of ventricular to auricular beats cannot be made out. After executing 81 such beats the ventricles suddenly stop and then gradually develop their usual rate, the durations of the successive ventricular cycles being in fifths of seconds—27, 21, 16, 13, 11, 9, 8, 7, 6, when the picture of typical complete block obtains with 142.5 auricular

and 42 ventricular contractions per minute. Many other long tracings were then made, but throughout all of them the block remained typically complete.

On the following day (5th May), during the course of eight long records, the heart irregularity we are here considering appeared only twice. The first instance occurred during the fourth revolution of the paper and while the heart-block was typically complete. The ventricular rate was 46.5, the auricular rate 123.7. The series of rapid ventricular contractions consisted of 27 systoles at the rate of 210 per minute. Fortunately this record (Fig. 11) was sufficiently clear to show that at this time the auricles were beating at a rate different to that of the ventricles and quite independently of them. The first ventricular cycle following this series of rapid beats lasted 3.6 sec., the next 3.2 sec.; here the record ends.

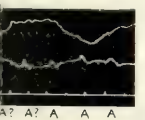
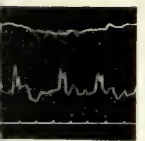
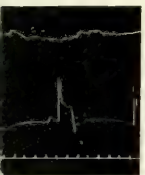
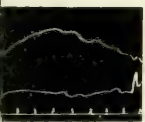
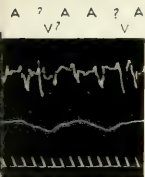
This irregularity was not again seen in the case of Dog No. 12 although the animal was under observation 278 days longer, during which time hundreds of tracings were made.

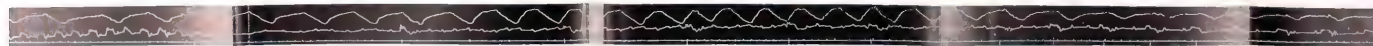
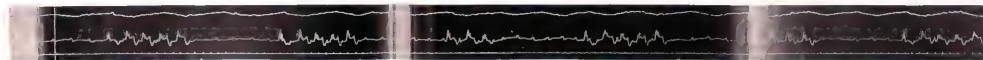
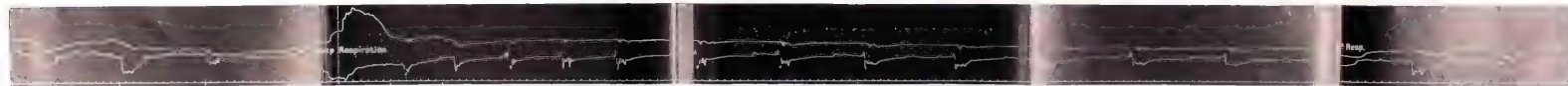
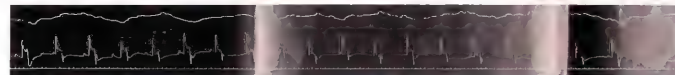
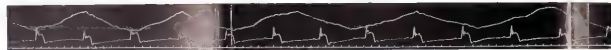
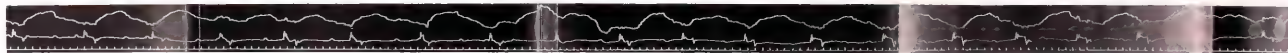
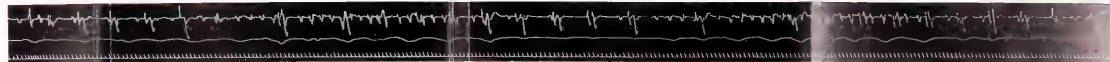
In the case of Dog No. 8 ventricular group irregularities of the kind under consideration were encountered from the second to the fifth days, inclusive. They were not present on the first day, nor were they again seen after the fifth day. Since at this time the animal's chest was encased in dressings we are dependent entirely upon femoral sphygmograms for our data.

On the first day (second of block) the irregularities consisted mainly of comparatively long groups of rapid and rather irregular pulses followed by stoppage and the development of a slow pulse rate. The following analysis of one group (Fig. 12) will serve to illustrate the general features of the irregularity of this day. Following a series of rapid and irregular pulse waves 62 regular waves were recorded at the rate of 54 per minute. There was then an abrupt increase in the rate of the pulse to 153 per minute. With the fifty-fifth wave, however, the pulse stops, for, in all probability, about $6\frac{1}{4}$ sec.. Of this figure we cannot be absolutely certain, since the record is marred by the restlessness of the animal that appeared toward the close of the period of stoppage. This period is succeeded by one in which the pulse rate gradually increases through about seven waves, the duration of successive cycles being in seconds—2, 1.8, 1.6, 1.5, 1.4, 1.4, 1.2, when, until the end of the record, the waves recur perfectly regularly and at the slow rate of 52.8 per minute.

At other times on this day, however, the heart beat was very much more irregular, indeed, it was so irregular as not to lend itself well to description. A reproduction of one of the tracings of the irregularities must therefore serve to illustrate their characteristics (Fig. 13).

Irregularities similar in kind to those just referred to were again seen on the second and third days, but they were relatively infrequent, and in their place we find mainly short groups of rapid beats separated by pauses of varying lengths. Sometimes over long periods of time there are regular groups consisting of two waves in close proximity to each other (Fig. 14).





The pauses between these groups may be longer than, or regularly shorter than, twice the interval subtended by two of the rapid waves. Again, the groups may consist of a large number of beats, when they are usually less regular. The pauses between them may be brief or they may be as long as 6 sec..

On the fourth day, the arrhythmia was infrequently seen and consisted only of the regular form seen on the first and second days.

The type of irregularity illustrated in Figs. 13 and 14 simulates very closely pictures frequently seen in partial heart-block where regularly recurring ventricular silences are met with or where there recur abrupt stoppages and recovery of the ventricles from and to some stage of partial block respectively. In the absence of a record of auricular beats their identity cannot be positively denied. Nevertheless there is sufficient circumstantial evidence to practically prove that the block at these times was complete and that the cause of the irregularity is, therefore, to be sought for in the independently contracting ventricles. This evidence follows:—(1) A similar irregularity was seen in the case of Dog No. 12 while the block was obviously complete; (2) When each group consists of two beats, the long interval we have seen may be somewhat less than, or somewhat greater than, twice the short period. It is well known that were this irregularity caused by regularly recurring ventricular silences, the longer pause would regularly be somewhat less than twice the shorter beats; (3) Furthermore, where the group consists of three pulses followed regularly by a pause the interval between the second and third ventricular systoles of the group is usually shorter than that intervening between the first and second. In an irregularity of the type caused by partial heart-block the successive ventricular cycles would lengthen rather than shorten.

In the case of Dog No. 11 this type of group beating was met with under the same circumstances as in the case of Dog No. 8, and we, therefore, again have only sphygmograms for the analysis of the condition.

The irregularities were seen on but two days, namely, the third and fourth. On the third day (first of the irregularity) it consisted almost exclusively of long periods of rapid pulse waves followed by pauses often lasting as long as 8 sec.. The pause was succeeded by a gradual development of a slow rhythm which rarely lasted longer than a few beats, when the pulse rate again became rapid. The rate when rapid was 126 per minute. It was not slow long enough on this day to permit of an estimate of the rate at such times.

On the second day, the irregularity consisted exclusively of a few rapid beats, 2, 3, or 4, separated by pauses. At times the pulse was typically slow over long periods; then the pulse rate was 35.3 per minute. For reasons given above, we are of the opinion that in this case, too, the block was always complete, although at places the irregularity simulated one of the lower grades of partial block.

Our experiments throw no light upon the cause of this interesting type of group beating of the ventricles. It would, however, appear, from some experiments which one of us has performed, that irregularities resembling some of those described here may be obtained by alternately warming and cooling the region of the auriculo-ventricular bundle (no other parts of the heart have been tested) in the ventricles of the excised heart while they are contracting independently of the auricles'. Should the ventricles happen to be quiescent, warming the auriculo-ventricular bundle up to 38° or 40° C. may start a series of beats, which may continue until the warmth is withdrawn or until the same region is cooled. The result can be obtained regularly only when the re-activity of the heart is lowered by the temporary cessation of perfusion. It would appear that group beating may also be obtained in the case of the frog's heart by asphyxiation of the spontaneously beating ventricle¹³.

As to the cause of the appearance of the group beating in our cases of experimental heart-block, we have not the slightest clue. The fact that it appeared shortly after the operation upon the heart in the case of Dogs Nos. 8 and 11 would seem to indicate that it had been brought on by local irritation. It is, however, difficult to reconcile with this view the fact that in the case of Dog No. 12 the irregularity appeared suddenly and quite unexpectedly, and that it disappeared quite as abruptly, in the midst of the perfectly even course of the disease. The fact that while Dog No. 12 was subject to this irregularity, it could be brought on by exercise (see below) should suggest the possibility of a participation of the accelerator in its production. It is conceivable that accelerator impulses might under certain circumstances exert the same influence upon the independently beating ventricles as does warmth applied to the auriculo-ventricular bundle.

Symptoms associated with group beating of the ventricles.—Very obvious symptoms were associated with this type of ventricular irregularity. On the very first day of the irregularity, after some tracings had been made, Dog No. 12 was placed upon the floor and closely observed. He ran about for some minutes in his usual lively manner, then stood still, looked about anxiously, spread his legs, evidently in order to maintain his equilibrium, swayed from side to side in a conscious effort to keep his feet, but within a few seconds became perfectly normal and happy again.

On the following day (4th May) an effort was made to discover some method of inducing the attacks of irregularity. While the animal was lying quietly upon its side, and while the heart beat was being recorded, he was startled by loud noises, or his breathing was interfered with by occluding his nostrils up to the point of restlessness, but all to no avail. The attacks of irregularity that were recorded bore absolutely no relation to the procedures of the experiment. Then the animal was placed upon the floor and induced to take vigorous exercise (running). The pulse was felt at the moment he came to rest and was usually found to be rapid; after some moments ventricular stoppage occurred. With it the animal looked about anxiously

but did not fall. On the third day the irregularity could not be induced by any of the measures tried.

In the case of Dog No. 8, during the periods of stoppage, the animal, when up and about, became unsteady on his legs but never lost consciousness or the ability to support itself in the standing posture. When stoppages lasting as long as 7 sec. supervened, while the animal was lying quietly upon the table, a certain amount of restlessness became manifest.

Dog No. 11 had striking symptoms, probably because the ventricular stoppages in this case were the longest observed, and because of his weakened state, the result of purulent pericarditis. In case the stoppages lasted 7 to 8 sec., the animal usually lost consciousness, and was seized with epileptiform convulsions. The behaviour of the animal during such attacks is depicted in the following extract from our protocols :—

“The animal had a perfectly typical epileptiform seizure while we were counting the pulse in the femoral artery. While the animal was sitting quietly the pulse rate was about 120 per minute, and slightly irregular. Suddenly the pulse stopped, the respiratory rate increased, the animal gazed about anxiously, and, after there had been no pulse for about 7 to 8 sec., fell on to its side. A moment later the legs became rigid in the position of extension. This was soon followed by clonic convulsions affecting all of the extremities, succeeded again by tonic convulsions with typical opisthotonus and rapid stertorous breathing. Then the pulse began to beat rapidly, whereupon the animal recovered, first gazing about as though dazed and then resting comfortably.” In other attacks it was noted that when the femoral pulse fails, perfectly regular and rapid pulsations may be seen in the neck. Undoubtedly these were produced by the auricles which probably continued to beat regularly throughout.

It should be added here that the syncopal attacks and epileptiform seizures of our dogs are symptomatically identical with those which have been seen in cases of Stokes-Adams disease in man, and we believe that examination of the literature of the subject will show the cardiac signs of the attacks, in certain of the cases, at least, to be the same in man as in the dog. In the dog the faintness and the convulsions are both the result of the cessation of the circulation from causes resident in the heart itself, although it is possible that slowing of the ventricles may in part be determined by impulses arising in the cardiac centres. There is no reason for adhering any longer to the view that the epileptiform seizures, at least those associated with the rhythmic type of ventricular irregularity, point to the brain as the primary seat of the lesion that causes Stokes-Adams disease.

It is, however, conceivable that in cases of heart-block an exaggeration of the type of rhythmic irregularity which we have described on p. 191, and which in all probability is determined by rhythmic variations in the irritability of the medullary centres might, in animals, as well as in man, cause faintness or even convulsions. In such a case, however, the slowing of the ventricles and the convulsions would not be directly determined by

one and the same excitant; rather the temporary inefficiency of the medullary centres, by slowing the ventricles, would be the cause of anæmia of all parts of the brain whence the faintness and convulsions. Whether or not a single lesion within the central nervous system can directly, and at one and the same time, cause auriculo-ventricular dissociation with the irregularities we have described, and epileptiform convulsions, is a question with which we are not at present concerned*.

General symptoms of the cases of complete heart-block.

The remarkable feature of uncomplicated heart-block in the dog is the usual total absence of recognisable symptoms. Excepting, perhaps, a slightly increased susceptibility to fatigue, which may in large part have been the result of prolonged confinement, the animals appeared to be perfectly normal and happy. The young animals grew and increased in weight; indeed, one of them, No. 12, became abnormally fat.

Syncopal attacks were of exceedingly rare occurrence. The Cheyne-Stokes type of ventricular slowing of a severe grade was seen for only a few days in the case of Dog No. 7; the ventricular type for from two to four days in the case of Dogs Nos. 8, 11, and 12; while Dog No. 13, during his life of 343 days, could at all times have passed for a perfectly normal animal had there not been present the cardiac signs of heart-block.

Mode of death and autopsy findings in general.

Dog No. 11 died of purulent pericarditis on the sixth day; death in this instance was not unexpected. Dog No. 13 was killed on its 343rd day, after having been the subject of certain tests, to which reference will be made below. Dogs Nos. 7, 8, and 12 died quite unexpectedly on their 28th, 92nd, and 320th days respectively. The deaths occurred at night and without any premonitory symptoms whatever. Daily cardiograms up to the very day of death in the case of Dogs Nos. 7 and 8 gave no indication of approaching dissolution. *At autopsy* (for details see protocols) marked pulmonary œdema was found in Dogs Nos. 7 and 8; it was present, though slight, in the case of Dog No. 12. Dogs Nos. 8, 12, and 13 had extensive adhesive pericarditis, while in Dog No. 7 the layers of the pericardium were adherent only over the upper parts of the heart.

A comparison of the heart weight with the body weight (see Table IV) shows that hypertrophy of the heart is of regular occurrence and may amount to as much as 100 per cent. of the estimated normal weight of the heart.

* The effect upon the heart of direct stimulation of the vagus was tried on the 80th and 75th days of Dogs Nos. 8 and 13 respectively. The results have been reported in full in another connection, and therefore need not be mentioned here⁸.

TABLE IV. Showing the relation of heart weight to body weight.

| NO. OF DOG. | DURATION OF LIFE. | BODY WEIGHT AT END IN K. | HEART WEIGHT IN GRM. | NORMAL HEART WEIGHT (ESTIMATED).* | PER CENT. HYPERTROPHY. |
|-------------|-------------------------|--------------------------------|-------------------------|---|---------------------------|
| 7 | 28 | 7.7 | 72 | 58.6 | 23.8 |
| 8 | 92 | 9.2 | 140 | 68.4 | 105.0 |
| 12 | 320 | 23.9 | 300 | 177.6 | 69.0 |
| 13 | 343 | 17.5 | 200 | 130.0 | 54.0 |

* For this calculation the factors of Joseph (Journ. of Exper. Med., 1908, x, 527) have been employed, namely, 7.43 grm. of heart per K. of male, and 7.61 grm. per K. of female.

In each heart there was found at autopsy a scar, often calcified, involving a small part of the auriculo-ventricular junction just posterior to the *pars membranacea septi*. It was evident to the unaided eye that these scars lay in the path of the auriculo-ventricular bundle. Nevertheless, since the most important conclusions of this investigation are based upon the premise that the operation has affected the auriculo-ventricular bundle, we have not rested with this macroscopic evidence, but have in addition submitted the tissues in question to a rigid histological examination. These examinations were made by E. K. Cullen and by Wm. S. Miller, whose reports are given below.

Histological findings.

It is to be regretted that some of the material was spoilt. Owing, in some instances, to calcification of the scars, the most important sections of the specimens were lost. The perfect series of sections obtained from the hearts of Dogs Nos. 12 and 13 show clearly that in these cases none of the auriculo-ventricular bundle had escaped destruction. An imperfect but adequate series from the heart of Dog No. 8 shows that possibly in this case a few fibres of the auriculo-ventricular bundle still persisted.

Methods.—The blocks received from the hearts of Dogs Nos. 12 and 13 were fixed in Tellyesniczky's fluid, embedded in celloidin, cut serially in sections μ 20 thick, and stained with hæmatoxylin and eosin."

Results.—In the case of Dog No. 12 the destruction of His' bundle is complete, the absence of muscle bundles is first noticed at a point just below the posterior leaflet of the aortic semilunar valve, and just above the complete fusion of the median leaflet of the tricuspid valve with the *septum membranaceum*. The destroyed area is about 1 mm. in width. The same results are found in the case of Dog No. 13, but in the case of Dog No. 8 (sections cut by E. K. Cullen) the bundle is not completely destroyed, since a few bundles of heart muscle containing 8 to 12 muscle cells can be readily followed through the line of crush. These bundles do not present the characteristics of regenerated muscle, but appear to be in all respects like the surrounding heart muscle. In the case of Dogs Nos. 12 and 13 blood vessels

could be traced through the line of crush, but I failed to find any nerves." (W. S. M.)

The important parts of the blocks from Dogs Nos. 7 and 11 were valueless on account of tearing and breaking on cutting.

Relation of respiratory to ventricular rhythm.

Every one of the cases of complete block presented at times a remarkable cadence, usually 1 : 1, of the respiratory and ventricular rhythms. At such times the beginning of ventricular contraction precedes by a very short interval the beginning of inspiration. This is the case in the vast majority of instances in which the cadence has been observed (see Fig. 16). Much less frequently it happens that ventricular relaxation shortly precedes expiration (Fig. 17). Still more rarely there occurs a periodic shifting from one to the other of the two above-mentioned types, so that for a while ventricular contraction just precedes inspiration, the relation then shifting through one or several respirations until ventricular relaxation just precedes expiration (Fig. 18). With about the same degree of rarity the ventricular activity shifts irregularly in the period of inspiration. The accompanying diagrams (Fig. 19) will serve to illustrate these facts. They show the position of ventricular contraction (*c*) or of ventricular relaxation (*r*) with respect to the two phases of respiration, each letter representing the relation as it occurred more or less regularly throughout the record of one day each in three cases.

This ventriculo-respiratory rhythm probably obtains only when the uninfluenced rates of the ventricles and respirations are approximately alike. Furthermore, the relation is not absolutely constant, but is readily altered by such conditions as normally affect the rate of the ventricles and, especially, of the respirations. But whenever, for example, the respiratory rate for some reason or other changes while the 1 : 1 cadence is manifesting itself, it usually happens that within a very few beats the cadence is re-established. The same re-establishment may also occur when the rate of the ventricles is abruptly altered. A beautiful instance of such a readjustment occurred during one of the syncopal attacks of Dog No. 8 (see Fig. 12). The tracing shows that while the block was typically complete, and while the ventricles were beating slowly, the 1 : 1 cadence was exact, ventricular systole just preceding inspiration. With the onset of the rapid ventricular rate the respiratory rate decreases. Now, and as long as the rapid ventricular rate continues, no regular relation can be made out between the respirations and the ventricular beats. When the ventricles begin to beat subsequently to their stoppage there seem to be two respirations in each of the first four cycles, although of this we cannot be certain. But as the ventricular rate increases this relation disappears to be replaced after a lapse of only four cycles by a permanent 1 : 1 ventriculo-respiratory rhythm simulating in every respect the rhythm that obtained before the heart became irregular.

The factors upon which this ventriculo-respiratory rhythm depends are not clear and will remain so until it can be made the subject of direct investigation. It would require too much space to discuss all of the possibilities in the case. We may, however, say that, of the many possible factors which may play a rôle in determining this synchronism, we are of the opinion that the all-important one is the effect of some movement of the heart upon

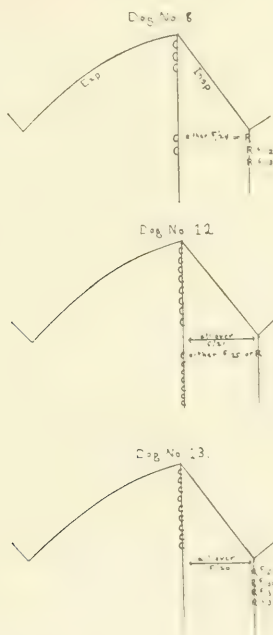


Fig. 19. $\times \frac{1}{2}$ linear. Diagrams showing the relation of ventricular contraction (C) or relaxation (R) to the phases of respiration in most of the instances of 1:1 ventriculo-respiratory cadence in the case of Dogs 8, 12, and 13. The vertical lines are time abscisse and are drawn to indicate the moment of change from the phase of expiration to that of inspiration and from inspiration to expiration. The numbers show the dates when the relation opposite which they stand were observed; thus 612, e.g., means June (sixth month) twelfth day.

the Hering-Breuer fibres in the lungs. That this is the important factor is indicated by the observation that contraction late in expiration seems to determine inspiration, whereas the opposite motion of relaxation occurring late in inspiration seems to determine expiration.

A study of tracings of cardiopneumatic movements published by Haycraft and Edie¹¹ seems to throw some light upon the former relation, in that there occurs in association with ventricular systole a slight expiratory movement of air and therefore a slight diminution in the size of the lungs. It seems possible that it is this expiratory movement occurring late in expiration that, in our experiments, cuts short expiration and inaugurates an inspiratory movement. This first expiratory movement on the cardiopneumogram is followed by an inspiratory movement which continues until ventricular relaxation begins. We are not at all convinced that this phase of the cardiopneumatic movements explains the instances in which we found ventricular relaxation to just precede expiration.

It should be added that the relation between ventricular and respiratory activities here noted has been seen in one of our cases of heart-block in man.*

Final experiment on Dog No. 13.

It was hoped when this research was planned that we would have the opportunity of confirming, and of adding to, the results obtained from the indirect study of the circulation which has occupied the preceding pages of this paper by a study by more direct methods of observation of at least two of our cases of chronic heart-block. But all of the animals, with the exception of No. 13, died suddenly before we thought the proper time had arrived for the final experiment. Nevertheless, the results obtained from the study of this one animal are of sufficient interest to warrant their presentation in full.

On his 343rd day, Dog No. 13 (the animal had not had a bad symptom during all of this time, nor any marked ventricular irregularities) was prepared for operation. In the first place several preliminary tracings were made for the purpose of determining the rate of auricles and ventricles before the operation. The auricular rate was slow and rather difficult to estimate correctly. We, however, believe it was about 67.5 per minute; the ventricular rate at the same time was 37.5. Morphine, 1½ gr., was then given subcutaneously. Tracings made one hour later showed the auricular rate to be even slower than before and still difficult to estimate; only four waves could be made out in 8 sec. of record. At the same time the ventricular rate had decreased to 33 per minute. The animal was placed upon the operating table and etherised. The ether was taken without a struggle. When the animal was fully anaesthetised the ventricular rate was found to be 49.5, whereas the auricular rate apparently was about the same as before. After having inserted the tracheal cannula it was found that the ventricular rate had increased still further—it was 54 per minute. The auricular rate had increased to 127.5 per minute.

These few figures we regard as extremely instructive, since they show, more clearly than any other consecutive records we have made, the independent reactions of the two regions of the heart to the same set of conditions.

* Dr. Thomas Lewis informs us that it occurs as a rule in chronic heart-block and that it has been frequently noted.

TABLE V. Showing an instance of the independent reactions of the auricles and ventricles.

| PROCEDURE | RATE PER MINUTE OF | | REMARKS. |
|-------------------------------------|--------------------|------|---------------------------|
| | A. | V. | |
| Normal immediately before operation | 67.5 | 37.5 | A rate approx. only. |
| One hour after 1½ gr. morphin. | slower | 33.0 | Only 4 A waves in 8 sec.. |
| Under ether | same | 49.5 | |
| After insertion of tracheal cannula | 127.5 | 54.0 | |

Morphine (Table V) slows both the auricles and the ventricles, the subsequent administration of ether accelerates the ventricles only, while now injury to tissues causes a further acceleration of the ventricles and accelerates the auricles too.

It is useless to speculate as to the cause of this independence of the reactions of the two parts of the heart, since the conditions we are dealing with are far too complex to allow of ready analysis. We may, however, assume that they are in part due to the relative immunity of the ventricles to vagus effects and in part to differences in the parts affected, both central and peripheral, by the factors determining the changes in rate.

After inserting the tracheal cannula, and while continuing the ether anaesthesia through it, the right jugular vein was freely exposed, both vagi were laid bare, the left cut and both ends prepared for stimulation, and the femoral artery was connected with a calibrated Hürthle spring manometer. During the following procedures, records were made on the Hürthle kymograph of the arterial pressure together with base line, heart beat (cardiograph), respiration, time in fifths of seconds and signal. Later the heart was freely exposed by the usual method and most of the procedures were repeated while recording the contractions of the right auricle and right ventricle directly by means of tambours. The left accelerator was also prepared for stimulation. The results obtained in the two stages of the experiment will be presented in logical order rather than in the order of the experiment.

(1) *Normal record.*—(a) This record is of significance mainly in showing the exact arterial pressure in a case of heart-block in the dog. The systolic was 190, the diastolic 50 mm. Hg.. These values should be compared with the normal femoral pressures (aortic end pressures) of the dog, 188 and 95¹, and with the brachial pressures (lateral aortic) of man, both normal, 111 and 74, and with complete heart-block, 118 and 61². It is interesting to note the relatively slight differences in the values of the systolic pressures in complete block and during normal heart action, both in the dog and in man, as compared with the relatively large differences in the diastolic pressures in both. These data illustrate the necessity of estimating both the systolic and diastolic pressures in clinical studies in blood pressure. At the same time the observation serves to indicate the substantial accuracy of the methods of making these estimations in man.

(b) The picture presented by the exposed heart was similar in every way to that seen when heart-block is acutely produced.

(c) The tracings obtained directly from the heart justify in every particular the method of studying the movements of the heart which was used throughout the whole of this research.

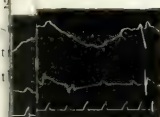
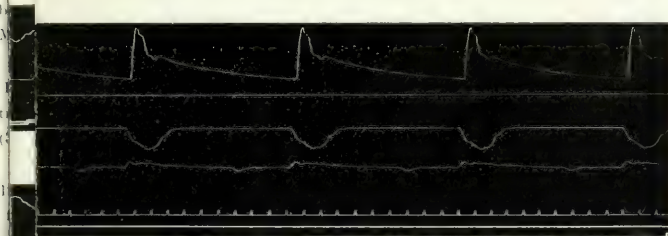
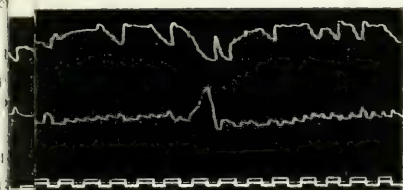
(2) *Stimulation of the peripheral end of the vagus.*—The results of this experiment have been considered in detail in another place². Here we may merely call attention to the fact that a weak stimulus, but one that suffices to practically stop the auricles, is without decided effect upon the ventricles, although the strongest stimulation reduces slightly the rate of the ventricles. And whereas the effect upon the auricles is immediate, the ventricular beats do not lengthen until from 3 to 5 have been inscribed, the maximum slowing being reached comparatively late and at a time when the auricular rate is increasing.

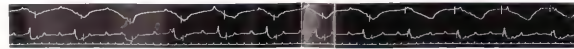
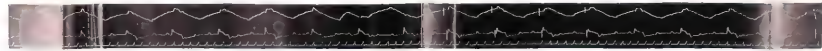
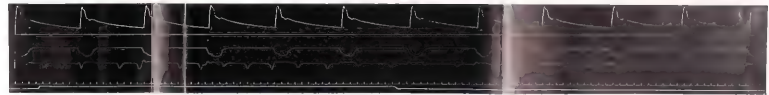
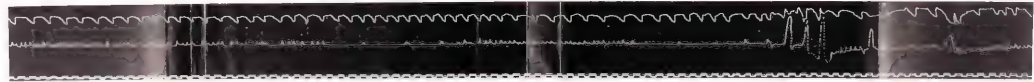
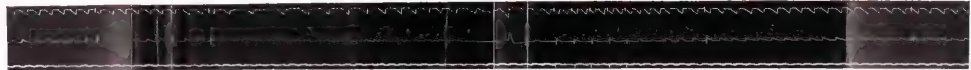
Strongest vagus stimulation has but a slight effect upon the blood pressure. With closed thorax both pressures are lowered only 5 mm.. With the thorax open they are lowered 20 to 30 mm. Hg..

(3) Stimulation of the accelerator nerve (shielded electrodes) late in a prolonged experiment caused a greater proportional acceleration of the ventricles—from 44.3 to 53.9 per minute, or 22 per cent.—than of the auricles—95.6 to 111.1 per minute, or 15.5 per cent. The blood pressure increased with the acceleration.

(4) Stimulation of the central end of the left vagus, the right vagus and both accelerators being intact, caused, with feeble currents, marked slowing of the auricles, whereas the rate of the ventricles was not affected. The respirations ceased. The effect upon the ventricles of stronger stimulation is shown by the following figures which are, in fifths of seconds, the durations of successive groups of five ventricular cycles each: 28.2 (immediately before stimulation), 28.5, 29 (slowing becomes distinct in the ninth ventricular cycle), 29.5, 30.5, 32, 31.5 (respirations are resumed here), 31.5. The ventricular slowing is slight and begins later than the auricular slowing. The blood pressures are at first increased slightly, but soon there succeeds a decided and lasting fall. During or shortly after stimulation the one to one relation of auricles and ventricles described on p. 193 was occasionally seen. The auricular wave in these places (see Fig. 20) appears quite regularly in the latter half of the ventricular cycles, never immediately after a ventricular contraction. This observation serves to support the explanation of this phenomenon as seen in the intact animal, which was suggested upon another page (194), namely, that it is due to a high vagal tone which diminishes temporarily in each ventricular cycle.

(5) Stimulation of the central end of the saphenous nerve never resulted in anything but slight and insignificant acceleration of auricles and ventricles as well as of the respirations.





(6) Stimulation of the central end of one vagus after section of both caused an insignificant slowing of the auricles 141.6 to 138.6 and a decided but irregular acceleration of the ventricles, the successive ventricular cycles lasting, in fifths of seconds, 9, 10.6, 9.4, 9.6, 9.5 (stimulation begun), 10.2, 10, 9.7, 9.2, 7.4, 7.4, 8 (stimulation ended), 6, 8.4, 9, 7.2, 10.1, 7.3, 5.2, 8.2, 7, 9.7. With the eighth ventricular cycle the blood pressures began to rise.

(7) The effect of digitalis has been recorded in another place.

Relatively complete heart-block with recovery.

In the case of Dog No. 3 we produced at the operation what appeared to be complete heart-block, but in the course of twenty-six days the conductivity, to all appearances, became normal again. This case is an interesting one, and since, in addition, it will be essential for the reader to know the progress of the animal from day to day before the results can be intelligibly discussed, we shall first record in full the protocols of the experiment.

Dog No. 3.—Young, but large, setter. Operation 21st February, 1906. The third time the hypodermic needle was inserted into the ventricle complete block resulted and lasted as long as the heart was exposed to view. Another operation, which does not concern us here, was performed upon the heart at the same time. Before the wounds were bandaged the pulsations, which could be seen in the veins of the neck, led us to suspect that the auriculo-ventricular rhythm was 3:1, and later 3:1 with occasional 2:1 cycles. The operation was concluded at 1.0 p.m.

5.0 p.m. Pulse 72 per minute; beats occasionally dropped.

11.0 p.m. Pulse at first 56, but rate is occasionally doubled for a few beats. Finally the rate becomes 88.

| | | |
|--------------|------------|--|
| February 22. | 9.0 a.m. | Pulse regular and strong, 50. |
| | 2.0 p.m. | " " " 52. |
| | 9.0 p.m. | " " " 58. |
| February 23. | 9.0 a.m. | " 56. |
| | 12.0 noon | " strong, 44. |
| | 5.0 p.m. | " 45. |
| | 8.0 p.m. | " 45. |
| | 11.0 p.m. | " 53. |
| February 24. | 9.0 a.m. | " regular and strong, 72. |
| | 11.0 a.m. | " " 68. |
| | 12.0 noon | " " 76. Dog bright and comfortable. |
| | 2.0 p.m. | " 73. Severe bloody diarrhœa. |
| | 4.0 p.m. | " 80, occasional dropped beats. |
| | 7.0 p.m. | " 76. |
| February 25. | 9.0 a.m. | " 72. |
| | 12.30 p.m. | " 78. |
| | 6.0 p.m. | " quite irregular, there being occasional long pauses. |
| February 26. | 9.0 a.m. | " regular 73. Slight inflammation of right eye. |
| February 27. | 10.0 a.m. | " regular, 66. |
| | 1.0 p.m. | " slightly irregular, 68. |
| February 28. | | Pulse slightly irregular, 67. |

- March 1. 9.0 a.m. Pulse regular, 78.
— p.m. First dressing. Excepting one stitch abscess, wounds have healed *per primum*.
- March 2. First tracings of apex beat. Rhythm exactly 2 : 1, ventricular rate being 65.2.
- March 4. The dog had not had food for 24 hours. When given meat she attacked it voraciously. Soon she began to stagger, stopped eating, squatted on the floor and began to howl. The pulse was felt as quickly as possible; it was slow, but could not be counted because of the animal's restlessness.
- March 5. Tracings without time record show the rhythm to be 2 : 1 and 3 : 1. The As-Vs intervals of the 2 : 1 cycles gradually lengthen until the rhythm becomes 3 : 1, when the As-Vs intervals are short and the rhythm soon again becomes 2 : 1. These events are repeated over and over again. Muscular exercise causes distinct acceleration of the heart beat, the rhythm remains 2 : 1 for a time, but eventually gives way to the condition first seen to-day.
- March 6. Before exercise the rhythm is 2 : 1 with an occasional 3 : 1 cycle; while 2 : 1 the ventricular rate is 60. Immediately after exercise the rhythm is 2 : 1, the ventricular rate now being 71.4. Later, occasional 3 : 1 cycles occur. At another time there were for a while alternating 2 : 1 and 3 : 1 cycles. At this time the auricular rate was 142. Later in the same record the rhythm became 2 : 1; here the auricular rate is 121. Still later, with an auricular rate of 137, alternating 2 : 1 and 3 : 1 cycles were again registered.

On another record the rhythm at first was 3 : 1, then occasionally the ventricles contract between the second and third auricular contractions before their normal time, so that there are, for example, eight auricular waves per three ventricular waves. Later in the same record the auricles slow decidedly, and the rhythm becomes 2 : 1. And still later the auricular rate again increases and again ventricular systoles appear between the second and third auricular systoles. Similar results were repeatedly obtained.

- March 7. Tracings show alternating periods of 2 : 1 and 3 : 1 rhythms. Measurements show that toward the end of the 2 : 1 periods the auricular rate increases and the increase continues for some distance into the 3 : 1 period. The auricular rate slows again shortly before the 2 : 1 rhythm returns.

In another tracing the block is for the most part complete. An auricular systole may occasionally determine a ventricular contraction. Where the block is certainly complete the ventricular rate is 58, the auricular rate, 165. No cause could be discovered of this unusually rapid auricular rate.

- March 8. Rhythm for the most part is 3 : 1.

- March 9. (1) Effect of exercise. (a) While the animal is resting the rhythm is 2 : 1. The auricular rate gradually increases and soon the As-Vs intervals lengthen, until there results one 3 : 1 cycle. Then, for approximately 6 cycles, the ventricles contract before the third auricular wave; the block is, therefore, relatively complete. The ventricular cycles are here relatively long at first, but later shorten gradually until the rhythm becomes 2 : 1. This cycle of events is repeated over and over again.

(b) Immediately after exercise, the auricular rate is markedly increased. Every ventricular contraction is determined by an auricular contraction, the rhythm at first being mainly 3 : 1, later mainly 2 : 1. The ventricular rate is much faster than during rest. Later, as the auricles slow, the ventricles occasionally beat before the auricles as in earlier tracings.

- (2) Effect tested of subcutaneous administration of atropin. Records were made at least every five minutes until 1.10 p.m.; here only the significant results are given.

| | TIME OR NUMBER OF TRACING. | RATE PER MIN. OF A | | REMARKS. |
|-----------|---|-----------------------|------|---|
| | 1st. | 169.4 | 41.3 | The block is complete. |
| | 2nd. | 128.2 | 64.1 | Rhythm is 2 : 1. |
| | 3rd. | - | - | Qualitatively the same as second. |
| | 12.18 | - | - | Atropin, 1 mg. |
| | 12.21 | 152.3 | 59.6 | Apparently block usually complete. |
| | 12.25 | - | - | Ditto. |
| | 12.30 | 177.0 | 59.0 | 3 : 1. |
| | 12.47 | 177.0 | 59.0 | All 3 : 1 excepting two near middle of tracing; here the third A fails to stimulate V, and V beats spontaneously before the fourth A. These Vs are longer than usual. |
| | 1.0 | 179.1 | 59.7 | Still 3 : 1. |
| | 2.0 | 170.4 | 56.8 | Ditto. |
| | 3.30 | 159.9 | 56.4 | For the most part 3 : 1, becoming 2 : 1 at end. |
| March 12. | Effect of atropin again tested. | | | |
| | 10.38 | 125.0 | 62.5 | Rhythm is 2 : 1. |
| | 10.39 | - | - | Atropin 2 mg. |
| | 10.41 | 130.4 | 65.2 | 2 : 1 for the most part. |
| | 10.44 | 157.0 | 49.7 | Block apparently complete. |
| | 10.53 | 184.8 | 61.6 | 3 : 1 with long As-Vs interval. |
| | 10.59 | 189.9 | 59.9 | Block complete. |
| | 11.05 | 180.6 | 60.2 | 3 : 1. |
| | 11.25 | 176.4 | 58.8 | 3 : 1 changing to complete block. |
| | 11.45 | 168.0 | 56.0 | 3 : 1. |
| | 2.0 | 159.5 | 60.2 | For the most part alternating 2 : 1 and 3 : 1. |
| March 15. | Mostly 2 : 1 cycles with occasional complete dissociation. Where the auricular rate increases the rhythm sometimes becomes 3 : 1. | | | |
| March 16. | Rhythm 2 : 1 only, excepting immediately after exercise, when it is 3 : 1. | | | |
| March 19. | Heart beat is irregular. Usually there are groups consisting of two or three beats separated by long pauses. In each group the duration of the successive ventricular cycles decreases. Each ventricular beat is preceded by an auricular wave, but no auricular waves are manifest in the pauses. This irregularity persisted with some variability, until the animal's death on 23rd April. It was shown that the group beating was determined by the respirations. | | | |
| April 7. | Atropin was given at a time when the heart manifested the irregularity seen on 19th March. One of the first effects was to bring out occasional 2 : 1 cycles, the only ones seen since the onset of the group beating. This effect appeared at the moment the heart beat became perfectly regular, but before there was any considerable increase in rate. During the period of maximum acceleration the heart beat was perfectly normal. | | | |
| April 23. | Final experiment. Under morphin ether anæsthesia the heart was freely exposed. Its beat was found to be normal. Then, while recording the movements of the auricles and ventricles with tambours, the region of the auriculo-ventricular bundle was crushed with the heart clamp. Complete heart-block came on at once. Other details of this experiment have been published in another connection. | | | |
| | Autopsy. There is a large organized thrombus attached to the endocardium of the left ventricle at the lowermost point of attachment of the aortic valve, and about on the line of junction of the right with the posterior | | | |

leaflet. While cutting out a block of tissue (one presumably containing the field of the first operation) for histological examination, the knife passed through a small opaque mass in the septum of the ventricles. This was located quite close to the upper edge of the muscular septum, but there could be made out above it a layer of apparently healthy muscle about 1 mm. deep.

"Microscopically the bundle is present and shows practically no change. The surrounding tissue does, however, show marked inflammatory change." (E. K. C.)

Discussion.—The most important results of this experiment may be summed up in a few words: Heart-block was produced by the injection of a solution of iodine into the region of the auriculo-ventricular bundle. Immediately after deposition of the iodine solution in the ventricular septum the block was complete, but as soon after the operation as tracings could be obtained (nine days) the block was found to be partial or, at times, relatively complete. In the course of twenty-six days conduction from auricles to ventricles became normal.

The first question that presents itself here for consideration is—How was the recovery accomplished? Was it (*a*) the result of the regeneration in the auriculo-ventricular bundle of structures which had been destroyed by the operation, or was it (*b*) the result of the assumption of the function of conducting the cardiac excitation wave by some structure or structures other than those contained within the auriculo-ventricular bundle?

The second suggestion is invalidated by the final experiment, in which it was shown that compression of the auriculo-ventricular bundle again results in heart-block.

The first suggestion made above, namely, regeneration of the bundle, cannot be positively excluded when considered in the light of this experiment alone, but other experiments of this paper have demonstrated that functional regeneration of the auriculo-ventricular bundle does not take place after thorough destruction of a narrow section of it. We are therefore forced to conclude that the recovery of function was permitted through the removal of something that was interfering mechanically with the passage of the excitation wave through the bundle. This conclusion is supported by both the macroscopic appearance of the heart at autopsy and the microscopic appearance. These showed that the solution of iodine had been deposited in the ventricular septum, not in the bundle, but rather just below it. The bundle was probably at first compressed by the solution injected, and it is possible that the inflammation set up by the iodine contributed further to this pressure. The transportation of the iodine, of the products of necrosis formed by its action, and of the inflammatory exudate away from the region of the auriculo-ventricular bundle resulted in its gradual decompression with the restoration of its normal or almost normal functional capacity.

Another interesting feature of this case was the existence at many times of a condition which has been termed relatively complete heart-block. This is a condition in which the conductivity of the bundle is impaired, not completely interrupted, to such an extent that impulses arising in the auricles

reach the ventricles, it is assumed, but are of subminimal strength. The result is auriculo-ventricular dissociation. In this respect the condition resembles absolutely complete heart-block, differing from it in that a slight increase in the reactivity of the heart may, in the case of relatively complete block, effect a change from the condition of dissociation to one of the several stages of partial heart-block. And, it should be added, relatively complete block may develop from partial block when the reactivity of the heart diminishes. Effective changes in reactivity and consequently in the grade of block may be brought about, it is conceivable, by a slowing or an acceleration of the auricular rate, since this would be associated with an increase or a decrease, respectively, in the strength of the auricular impulses acting upon the ventricles.

In the case of the animal we are considering the conductivity of the auriculo-ventricular bundle was such, between the 5th and 15th March, inclusive, that slight alterations in state often resulted in the development of relatively complete from partial block and *vice versa*. Often it is not possible to discover the cause of the change, while at other times more or less plausible explanations suggest themselves. For instance, on 9th March, before the administration of atropin, there was complete auriculo-ventricular dissociation, the auricular rate at the time being 167.4; later, the auricular rate became 128.2, and the dissociation gave way to a 2:1 rhythm. Later in this experiment, while the auricles were beating at the rapid rate of 177+ beats per minute, the dissociation gave way to a 3:1 rhythm. The explanation we would offer of these apparently contradictory results is that in the first part of the experiment the auricles were beating so rapidly that none of the impulses reached the ventricles with a residual strength sufficient to act as efficient stimuli. The ventricles, therefore, contracted spontaneously and independently of the auricles. When the auricular rate decreased there was a corresponding increase in the strength of the impulse, so that every other one was adequate. Later, when the rhythm became 3:1, the impulses may have been stronger, perhaps, through removal of vagus influence, and the irritability of the ventricles may have been such that they could respond to every third one.

Again, on the same day, as may be seen in the lowermost tracing of Fig. 21, the auriculo-ventricular rhythm while the animal was at rest was 2:1. With a gradual increase in the auricular rate the As-Vs interval lengthens, until dissociation of beats preceded by one 3:1 cycle develops.* Evidently the spontaneity of the ventricles asserts itself now because the period of the ventricles is shorter than that which the enfeebled auricular impulses can determine. Why, then, does not the increase in the auricular rate induced by exercise (fourth tracing from bottom) now change the partial block into a relatively complete block as it did a moment earlier? Because, we believe, the increase in the rate of the heart beat with exercise is the result of accelerator action, and although such action might, it is true,

* On account of reduction of the figure, this does not appear.

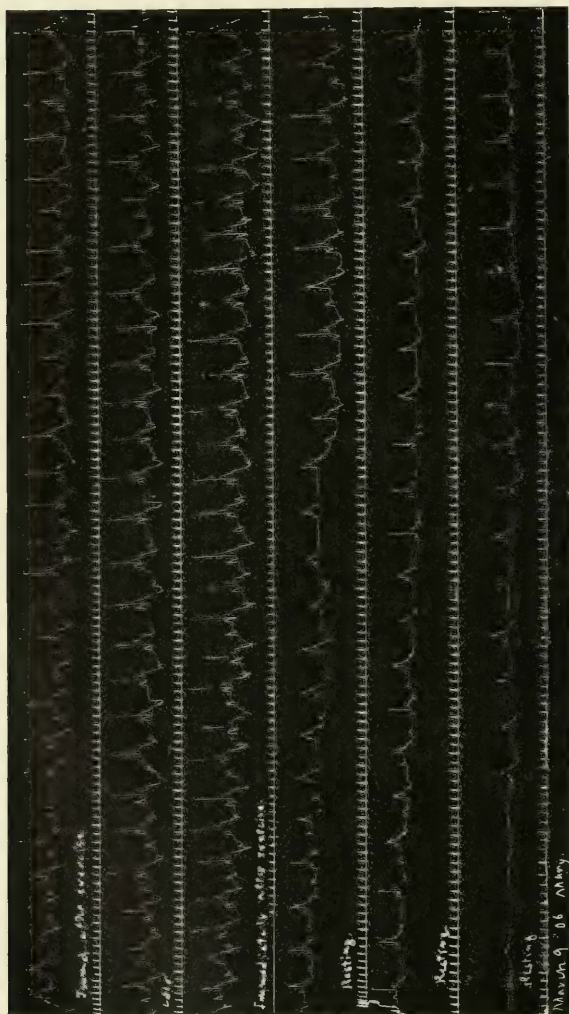


Fig. 21. $\times \frac{1}{10}$ linear. Showing several grades of partial and relatively complete block. Dog No. 3. For details see p. 215.

reduce the strength of the auricular impulses because of their increased frequency, it at the same time probably increases the reactivity of the ventricles, so that they can respond to every third or even to every second auricular impulse.

In the same tracings it may be seen (second tracing from bottom) that occasionally while the general rhythm is 2 : 1 the ventricles beat spontaneously. This happens, we believe, because the time occupied by two auricular beats is so nearly equal to the spontaneous periods of the ventricles that the latter may contract before the second auricular impulse reaches them.

Not infrequently the tracings show that the first ventricular cycle of a series of dissociated beats is the longest, that the successive cycles shorten until a constant rate is attained. This we believe to be a manifestation of the phenomenon termed, development of rhythm. While the ventricles are being driven by the auricles their inherent rhythmicity is depressed. It is therefore comparatively low at the moment the ventricles are freed of the influence of their pace-maker, and their rate of beat is consequently slow until the dormant rhythmicity becomes fully awakened.

Slight grade of partial block with complete recovery in 24 hours.

In the case of one of the dogs (No. 4) complete block resulted with the insertion of the hypodermic needle, but the heart rhythm became normal before the wounds were closed and while the heart was still exposed to view. On the day following the operation some doubtful evidence was obtained (see protocols) of the existence at times of a 2 : 1 rhythm and occasional ventricular silences. Later in the same day the pulse became perfectly normal and remained so as long as the dog was under observation.

At the autopsy, which was performed seventeen days after recovery, there was found in the right auricle a patch of vegetations about 1 mm. long and 2 to 3 mm. wide. This was situated slightly above, and parallel to, the auriculo-ventricular junction and a bit posterior to the membranous septum. No macroscopic lesion could be discovered exactly in the course of the auriculo-ventricular bundle.

The specimen was spoiled in cutting and no histological study could therefore be made.

SUMMARY.

Summarising, briefly, the more important results herein recorded, it may be said that by injuring practically nothing but the auriculo-ventricular bundle it is possible to produce chronic auriculo-ventricular heart-block in the dog. In case the destruction of the narrow segment of the auriculo-ventricular bundle is complete, or practically so, the block is complete, or eventually becomes so, and is permanent. In case the bundle is compressed, but not noticeably injured, the block may at first be either complete or partial, but disappears in the course of time.

Animals with complete heart-block exhibit many interesting heart irregularities the nature of which cannot be made clear in a summary.

Some of the cases of complete heart-block have syncopal attacks resembling symptomatically those seen in cases of Stokes-Adams disease, whereas others display no symptoms whatever.

CONCLUSIONS.

Previous experiments have shown that the auriculo-ventricular bundle constitutes the only functional connection between the auricles and ventricles in the dog. The present experiments confirm that conclusion and show further that there is present in the dog's heart no structure that can vicariously assume the function of the auriculo-ventricular bundle.

It may also be concluded from this research that the conducting structures of the auriculo-ventricular bundle do not regenerate. The significance of this conclusion from the standpoint of the theories of the heart beat is considered in another place⁹.

It would appear that there are at least two types of syncopal attacks in association with our cases of auriculo-ventricular heart-block. One type is probably not determined by central processes, whereas a second type, namely, that seen in association with Cheyne-Stokes respiration, probably depends upon the same factors as do the periodic respirations.

PROTOCOLS OF EXPERIMENTS.

Series I.—Experiments in which the attempt was made to produce heart-block by the injection of iodine into the vicinity of the auriculo-ventricular bundle.

Dog No. 1.—Young dog, small. Operation 19th February, 1906. After the fourth injection of iodine complete block was obtained. (Another operation was then performed which does not concern us here.) The pulse two hours after the operation was 82; five hours after, 160. Evidently the block had disappeared. The animal was found dead the next morning.

Autopsy.—Bloody extravasations found in the body cavities indicated that death was probably due to iodine poisoning.

Dog No. 2.—Large, young dog. Operation 20th February, 1906. Block was produced as in experiment 1, but the animal died two hours after the operation.

Autopsy.—Death was due to hæmorrhage through a hole in the auricle.

Dog No. 3.—See protocols in body of paper.

Dog No. 4.—Young, large spaniel. Operation 3rd March, 1906. After many trials we succeeded in getting complete block while injecting iodine, but finally broke the hypodermic needle. While closing the wound the rhythm became 1:1, but the operation could not be repeated because there was no other hypodermic needle available.

March 4.—Pulse cannot be counted because of playfulness of the animal. While he is in the recumbent position the pulse is regular and rapid; sitting, irregularities in the pulse occur, such as might well be associated with an alternating 2:1 and 1:1 rhythm. With the aid of this rough method it would seem that series of 2:1 beats alternate with series of 1:1; that immediately after exercise (walking) the rhythm is 2:1 for a time, changing then into alternating 2:1 and 1:1. Later in the day, immediately after throwing the animal, irregularities

of the pulse indicated 1 V silence in 2, then in 3, and then in 4 heart (auricular) beats. The dog would not remain quiet longer.

After this day the heart beat became regular and rapid. No signs of block were apparent.

Autopsy. —Slight old adherent pericarditis in the field of operation. A patch, apparently, of vegetations, about 1 cm. long and 2 to 3 mm. wide, was found in the right auricle slightly above the A-V junction, parallel to it, and a little posterior to the membranous septum.

Series II.—Experiments in which the attempt was made to destroy the auriculo-ventricular bundle by crushing it in the clamp passed into the septum by way of the aorta.

Dog No. 5.—Died on the table of hæmorrhage through the puncture in the aorta.

Dog No. 6.—Died on the table for some unknown reason after block had been successfully produced.

Series III.—Experiments in which the attempt was made to destroy the auriculo-ventricular bundle by crushing it in the clamp passed into the septum by way of the right auricle.

Dog No. 7.—Young dog. Operation 17th March, 1906. Before the operation the animal's pulse was 224 (excitement). Complete block was produced upon the first trial.

Immediately after operation, pulse 54.

Two hours after, pulse 36.

March 18.—a.m. Pulse 70; p.m. 60. Dog comfortable.

March 19.—a.m. Pulse irregular but very slow. Irregularities seem to be caused by extrasystoles, which occur with every second or third beat. Omitting the extrasystoles, the pulse rate is 60 per min.

P.M. Pulse sometimes quite regular, then it is 54 per minute.

March 20.—Pulse 54.

.. 21.— „ 66.

.. 23.— „ 66.

March 24.—First dressing. Wounds have healed *per primum*. Stitches removed. First cardiograms made.

| DATE. | | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|------------|--------|-----------------------|-----------------------|------------------|---|
| March 24 | .. | 137.7 | 59.0 | — | Block complete. |
| 25 | .. | — | — | — | „ „ No time record. |
| 26 | .. | 133.4 | 46.8 | — | „ „ |
| 27 | .. | 112.0 | 43.4 | — | „ „ V quite regular. |
| 28 | .. | 113.4 | 43.9 | — | „ „ |
| 29 | .. | 108.0 | 38.1 | — | „ „ very slight variations in V cycles. |
| 30 | .. | — | — | — | Same, but less marked. |
| 31 | .. | 79.8 | 37.8 | — | V fairly constant; A more variable. |
| April 1 | .. | 111.1 | 37.1 | — | Very slight variation in A and V. |
| 2 | .. | 97.2 | 34.7 | — | Same. |
| later.. | .. | 90.0 | 42.9 | — | Same. |
| 3 | .. | 101.1 | 39.1 | — | Same. |
| 4 | .. | — | — | Synchron. with V | Marked rhythmic variations in A and V. |
| 5 (a.m.).. | .. | 113.0 | 39.1 | — | No rhythmic variations. |
| (p.m.).. | .. | — | — | — | Marked rhythmic variations of A and V. |
| 6 (a.m.).. | .. | — | — | — | Slight rhythmic variations. |
| (p.m.).. | Irreg. | — | 37.9 | Periodic | Slight rhythmic variations of A. |

| DATE. | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|-------------|-----------------------|-----------------------|---|---|
| April 7 | Irreg. | 39.5 | — | No rhythmic variations. |
| 8 (a.m.).. | 97.4 | 37.7 | — | Slight rhythmic variations of A. |
| (p.m.).. | 121.0 | 42.4 | — | Very slight rhythmic variations in A and V. |
| 9 (a.m.).. | 116.8 | 37.9 | — | Rhythmic and synchronous variations in A and V. |
| (p.m.).. | 97.2 | 4.0 | Periodic | A and V slightly periodic. |
| 10 (a.m.).. | 63.4 | 36.3 | .. | Same. Rate for one respiratory period. |
| (p.m.).. | 95.0 | 42.0 | .. | A rather irregular in places. |
| 11 (a.m.).. | 67.5 | 38.0 | .. | Marked periodicity of A, less of V. |
| (p.m.).. | 101.3 | 42.9 | — | No rhythmic variations. |
| 12 (a.m.).. | 106.2 | 40.2 | .. | Periodicity of A. |
| 13 .. | ? | 48.2 | Synchron. with V | A somewhat irregular. |
| 14 (a.m.).. | ? | 41.3 | Periodic | A record not clear. |
| (p.m.).. | ? | 48.7 | Slightly Periodic. Generally synchron. with V | Variations in A not so marked as usual. |
| 15 (a.m.).. | — | — | — | Animal found dead. |

Autopsy. — The heart appears to be normal, except at two points where thrombi are adherent to the pericardium. One of the thrombi, 1 mm. high and about 3×2 mm. on cross-section, projects from the inner surface of the right heart along the line of attachment of the mesial cusp. The other thrombus is in the left ventricle directly opposite, along the line of insertion of the posterior leaflet of the aortic valve. It measures about 4 mm. in diameter. At the base of these thrombi the endocardium appears thickened and opaque. Both thrombi are situated at the posterior edge of the *pars membranacea septi*. There is marked pulmonary œdema.

Dog No. 8.—Young mongrel. Operation 20th March, 1907. After a few trials, complete block was obtained upon pushing hook into the ventricular septum. Within about 10 to 15 minutes the heart beat became normal. Only now was the tissue in the grasp of the clamp thoroughly crushed. Complete block preceded by stoppage of the ventricles was again obtained. Wounds were then closed.

| DATE. | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|---------------------|-------------------------|--|-------------------|--|
| March 20 (6.0 p.m.) | — | 60.0 | — | Pulse regular. |
| (10.0 p.m.) | — | 50.0 | — | |
| 21 (a.m.) | — | 50.0 | Synchron. with V. | |
| (p.m.).. | — | 150.0 (while rapid) 53.0 (while slow) | when slow | Pulse recorded with sphygmomanometer. |
| 22 .. | — | — | — | Group beating of V. |
| 23 .. | — | — | — | Groups of rapid and slow pulses. |
| 24 .. | — | — | — | Same. |
| 25 .. | — | 70.0 | Slightly periodic | Same. |
| 26 .. | — | 67.5 | Same | V regular. |
| 28 .. | — | — | — | Same. First dressing. |
| 29 .. | 168.7 | 61.9 | — | Wounds have healed <i>per primum</i> . |
| 30 .. | sl. irreg. 180.0 | reg. 65.0 | — | First cardiograms. |
| 31 .. | sl. irreg. 127.5 (?) | reg. 71.2 | — | Block complete. |
| | | | | V somewhat variable. |

| DATE. | | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP | REMARKS. |
|-------|-------|-----------------------|-----------------------|-------------------|---|
| April | 1 | 236.2 | 91.0 | — | V irregular, longest 1.2 sec., shortest 0.85 sec., |
| | 2 | 180.0 | 61.5 | — | V somewhat irregular. |
| | 3-8 | Not clear | 75 (about) | — | V somewhat irregular. Block certainly complete at most times, but in parts of one tracing rhythm may have been 2:1. |
| | 9-14 | 142-127 | 50-65 | — | V somewhat irregular. Block apparently complete. |
| | 15 | 135.0 | 65.0 | — | V sometimes rather rapid then tracing like 2:1; during long V cycles, block certainly complete. |
| | 16 | 97.0 | 62.0 | — | Same. A and V rates increase and decrease together. No relation to respiration. |
| | 17 | 146.2 | 33.7 | — | Irregularities not so marked. Block seems to be complete. |
| | 18 | 142.5 | 57.7 | — | More irregular, but block seems to be complete. |
| | 19 | 131.2 | 52.5 | — | V more regular. Block complete. |
| | 20 | 146.2 | 50.2 | — | A and V slightly irregular. Block certainly complete. |
| May | 21 | 172.5 | 56.2 | — | Occasional short Vs. Block apparently complete. |
| | 22 | 142.5 | 56.2 | — | V more regular. Block complete. |
| | 23-29 | 168.7-112.5 | 56.2-41.2 | — | Regular. Block certainly complete. |
| | 30 | 135.0 | 47.2 | — | V occasionally irregular. Block complete. |
| | 2 | 165.0 | 54.0 | — | V slightly irregular. Block complete. |
| | 3 | 172.0 | 49.5 | — | Regular. Block complete. |
| | 5 | 131.2 | 67.5 | — | A and V slightly irregular, both usually lengthening at same time. |
| | 6 | 165.0 | 54.7 | — | Regular. Block complete. |
| | 7 | 131.2 | 67.5 | — | V fairly regular. Block complete. |
| | 8 | 176.2 | 50.2 | — | Slight variations in V. Block complete. |
| | 9 | 157.5 | 48.0 | — | Regular. Block complete. |
| | 10 | 180.0 | 51.7 | — | V slightly irregular. |
| | 11-14 | 157.0-135.0 | 56.2-45.7 | — | Regular. Block complete. |
| | 15 | 165.0 | 47.2 | Synchron. with V | " " |
| | 16 | 172.5 | 51.0 | — | Fairly regular. Block complete. |
| | 17 | 123.7 | 51.7 | — | A and V slightly irregular. Block complete. |
| | 18 | 127.5 | 45.7 | Synchron. with V | V slightly irregular. Block complete. |
| | 19-21 | 153.7-120.0 | 49.5-41.2 | — | Regular. Block complete. |
| | 22 | 123.7 | 45.0 | Synchron. with V | A slower with respiration. V regular. Block complete. |
| | 23 | 142.5 | 47.2 | Slightly periodic | V slightly irregular. Block complete. |

| DATE. | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|-----------|-----------------------|-----------------------|---------------------|--|
| May 24 | 142.5 | 45.0 | Synchron. with V | A slightly periodic. Block complete. |
| 25 | 150.0 | 48.7 | — | — |
| 26 | 157.5 | 48.7 | Synchron. with V | Regular. Block complete. |
| 27 | 142.5 | 50.2 | — | V fairly regular. Block complete. |
| 28-June 2 | 153.7-142.5 | 43.5-49.5 | — | Regular. Block complete. |
| June 3 | 120.0 | 42.7 | — | A slightly periodic. |
| 4 | 135.0 | 43.5 | — | Regular. |
| 5 | 135.0 | 49.5 | — | Regular, before exercise. |
| 5 | 146.2 | 55.5 | — | Immediately after exercise. |
| 6 | 157.5 | 54.0 | — | Regular, before exercise. |
| 6 | 157.5 | 57.7 | — | Immediately after exercise. |
| 7 | 150.0 | 57.0 | — | Regular. Block complete. |
| | | | | Vagus exposed and stimulated. |
| | 161.2 | 105.0 | — | Under ether. |
| 8 | 165.0 | 67.5 | — | Regular. |
| 9 | 142.5 | 52.5 | — | — |
| 10 | 123.7 | 49.5 | — | A slightly periodic. |
| 11 | 127.5 | 45.0 | — | Regular. |
| 12 | 142.5 | 47.0 | Synchron. with V | Regular. |
| 13 | 142.5 | 44.2 | — | A slightly periodic. |
| 14 | 135.0 | 54.0 | — | Regular. |
| 15 | 165.0 | 56.2 | Panting | Temp. warm. |
| 16 | 138.7 | 48.0 | — | — |
| 17 | Indistinct | 54.7 | Panting | Temperature warm. |
| 18 | 150.0 | 45.7 | — | Regular. Temp. warm. |
| 19 | 157.5 | 45.0 | — | V slightly periodic. Temperature warm. |
| 20 | — | — | — | Found dead in a.m. For autopsy notes, see text. |

Dog No. 11. Small fox terrier. Operation 25th March, 1907. The first attempt to produce block was partially successful; block passed off while pericardium was being closed. It was opened again and block successfully produced.

March 25.—Immediately after operation (6.0 p.m.). Pulse is slow and regular.
8.0 p.m. Dog comfortable; slight dyspnoea; pulse 38.

March 26.—9.0 a.m. Quite comfortable; very slight dyspnoea; pulse 47.
9.0 p.m. Quiet and comfortable; pulse 48.

March 27.—Animal is having epileptiform convulsions of the kind described on p. 201.
Longest V stoppage 15 sec..

March 28.—Condition of heart described on p. 199. Some dyspnoea with expiratory grunt.

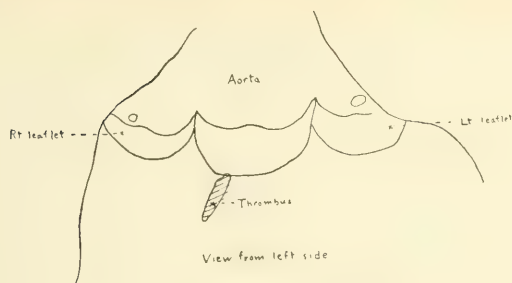
March 29.—Slight dyspnoea; stools slightly bloody; animal very sluggish; pulse 30 and regular; temperature 37° C.

6.0 p.m. Dog apathetic and drowsy; pulse 28 and regular; temperature 37.5° C.

March 30.—Found dead in the morning.

Autopsy.—Abdominal organs show evidences of venous congestion and there is a slight excess of peritoneal fluid. Lung adherent only in region of operation.

Extension sero-fibrinous pericarditis and mediastinitis with adherent pericardium. The interior of the heart seems to be normal everywhere, excepting where it apparently had been crushed. At these places small organized thrombi are attached. Their position and general form are shown in the accompanying sketches (Fig. 22).



View from right side.

Dog No 11.

Fig. 22.

Dog No. 12.—Large mongrel. Operation 26th March, 1907. Block successfully produced upon first trial. At the conclusion of the operation (6.10 p.m.), the pulse was 38 and regular.

| DATE. | A RATE PER MINUTE. | ART. PULSE PER MINUTE. | RESP. | REMARKS. |
|---------------------|-----------------------|---------------------------|--------------|---|
| April 27 (9.0 a.m.) | — | 50 | — | Pulse regular; dog comfortable. |
| (12.0 noon) | — | 46 | — | " " " |
| 28 (9.0 a.m.) | — | 42 | sl. dysp. | " " " |
| 29 (9.0 a.m.) | — | 34 | — | " " " |
| (2.0 p.m.) | — | 44 | — | but sluggish. |
| 30 (11.0 a.m.) | — | 50 | sl. laboured | Pulse regular; dog livelier; urine contains trace of albumen. |
| 31 .. | — | 36 | Better | Slightly irregular; some subcut. emphysema, but is lively. |
| March 1 (9.0 a.m.) | — | 55 | — | Regular; emphysema has largely disappeared. |
| (5.0 p.m.) | — | 52 | — | Regular; quite comfortable. |
| 2 (9.0 a.m.) | — | 55 | — | " " " |
| 3 (10.0 a.m.) | — | 54 | sl. dysp. | Regular; quite happy. |
| | | | | First dressing chest wound has healed <i>per primum</i> . |

| DATE. | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|---------|-----------------------|-----------------------|------------------|---|
| March 3 | 157.5 | 50.6 | — | First cardiograms; A and V regular. |
| 4 | — | — | — | Heart irregularity not clear on account of poor tracings. |
| 5 | — | — | — | Tracings not perfectly clear, but block is apparently complete. |
| 6 | 150.0 | 52.5 | — | Block complete. |
| 7 | 157.5 | 51.2 | — | " " |
| 8 | 172.5 | 50.0 | — | " " |
| 9 | 135.0 | 43.1 | — | " " |
| 10 | 135.0 | 45.0 | — | V regular. Block complete. |
| 11 | 135.0 | 39.0 | — | " " " |
| 12 | 150.0 | 51.0 | — | " " " |
| 13-17 | 135.0-150.0 | 38.2-48.7 | — | A and V regular. Block complete. |
| 18 | 150.0 | 45.0 | — | A slightly irregular. |
| 19 | 150.0 | 43.1 | — | " " " |
| 20 | 127.5 | 42.0 | — | Occasional long Vs; others fairly regular. Block complete. |
| 21 | 135.0 | 45.0 | — | Regular. Block complete. |
| 22 | 138.7 | 45.0 | — | " " " |
| 23 | 165.0 | 50.2 | — | " " " |
| 24 | 157.5 | 47.2 | — | " " " |
| 25 | 202.5 | 52.5 | — | " " " |
| 26 | 138.7 | 43.5 | — | " " " |
| 27 | 165.0 | 46.5 | — | " " " |
| 28 | 180.0 | 50.2 | — | " " " |
| 29 | 153.7 | 54.0 | — | " " " |
| 30 | 142.5 | 46.5 | — | Fairly regular. Apparently complete. |
| May 1 | 172.5 | 47.2 | — | Regular. Block complete. |
| 2 | 161.2 | 51.0 | — | " " " |
| 3-5 | — | — | — | Irregularity described on p. 195. |
| 6 | 157.5 | 42.7 | Synchron. with V | Regular. Block complete. |
| 7 | 146.2 | 42.7 | " | " " " |
| 8-12 | 157.0-176.0 | 42.0-54.0 | " | " " " |
| 13 | 161.2 | 50.2 | — | " " " |
| 14 | 165.0 | 44.2 | — | " " " |
| 15 | 172.5 | 49.5 | — | " " " |
| 16-19 | 142.0-165.0 | 41.0-46.0 | — | " " " |
| 20 | 165.0 | 47.2 | — | " " " |
| 21 | 161.2 | 42.7 | — | " " " |
| 22-24 | 142.0-146.0 | 36.0-37.5 | — | " " " |
| 25 | 150.0 | 36.0 | — | " " " |
| 26 | 157.5 | 43.5 | — | " " " |
| 27-30 | 146.0-157.0 | 31.5-45.0 | — | Regular. |
| 31 | 120.0 | 39.0 | — | Regular. Block complete. |
| June 1 | 157.5 | 44.2 | — | " " " |
| 2 | 157.5 | 49.5 | — | " " " |
| 3 | 142.5 | 39.7 | — | " " " |
| 4 | 161.2 | 37.5 | — | " " " |
| 5 | 153.7 | 50.2 | — | Immediately after exercise. |
| 6 | 142.5 | 46.5 | — | Immediately before exercise, regular. Block complete. |
| 6 | 172.5 | 62.2 | — | Immediately after exercise. |
| 7 | 150.0 | 50.2 | — | " |
| 8-11 | 146.0-161.0 | 34.5-42.7 | — | " |
| 12-14 | 150.0-157.0 | 45.0-53.5 | — | Regular. Block complete. |
| 15 | — | — | Panting | Record not clear. |
| 16-23 | 139.0-157.0 | 37.5-45.7 | — | Regular. Block complete. |
| 24 | 157.5 | 47.2 | — | " " " |

DIGITALIS EXPERIMENT.

| DATE. | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|---------------------|-----------------------|-----------------------|------------------|---|
| June 25 (3.54) .. | 172.5 | 45.7 | Panting | Regular. |
| (3.58) .. | 157.5 | 47.2 | .. | .. |
| (4.2) .. | 157.5 | 46.5 | .. | .. |
| (4.5) .. | 146.2 | 45.7 | .. | .. |
| (4.8) .. | — | — | .. | 0.5 cc. digitalin (Merck) 1 % intramusc. |
| (4.9) .. | 159.0 | 49.5 | .. | Regular. |
| (4.10) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.11½) .. | 154.5 | 53.5 | .. | Regular. |
| (4.12) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.13) .. | 159.0 | 54.0 | .. | Regular. |
| (4.15) .. | 144.7 | 48.7 | .. | .. |
| (4.17) .. | 136.5 | 46.5 | .. | .. |
| (4.18) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.19) .. | 143.0 | 48.0 | .. | Regular. |
| (4.21) .. | 137.2 | 45.0 | .. | .. |
| (4.23) .. | 121.5 | 42.7 | .. | Slight periodicity of A. |
| (4.24) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.25) .. | 123.7 | 42.7 | .. | Slight periodicity of A. |
| (4.27) .. | 133.5 | 42.7 | .. | Regular. |
| (4.29) .. | 135.0 | 45.7 | Panting | Regular. |
| (4.30) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.32) .. | 127.5 while fast | 42.0 | — | Sleepy; marked periodicity of A. |
| (4.35) .. | 127.5 | 40.5 | — | One V extrasystole. |
| (4.39) .. | 122.0 | 43.5 | Panting | Awake. Regular. |
| (4.40) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.43) .. | 118.5 | 45.7 | — | Slight periodicity of A. Two V extrasystoles. |
| (4.47) .. | 127.5 | 45.7 | Panting | Regular. |
| (4.49) .. | 127.5 | 47.2 | .. | A slightly periodic. |
| (4.51) .. | 117.0 while fast | 39.7 | .. | A more periodic. |
| (4.52) .. | — | — | .. | 0.5 cc. digitalin. |
| (4.54) .. | 129.0 | 45.0 | .. | A slightly periodic. |
| (4.57) .. | 114.0 (?) | 43.5 | Panting | A decidedly periodic. |
| (5.3) .. | 125.2 | 46.5 | .. | .. |
| (5.6) .. | 42.7 (?) while slow | 42.7 | .. | Beautiful periodicity of A. |
| (5.11) .. | 107.4 while fast | 39.7 | — | — |
| (5.11) .. | 42.7 while slow | 42.0 | — | |
| (5.11) .. | 117.0 while fast | 36.7 | — | — |
| (5.15) .. | — | — | .. | Same as at 5.11. |
| (5.20) .. | 137.2 | 46.5 | .. | After light exercise. Very slight periodicity. |
| (5.28) .. | 132.0 while fast | 32.2 | — | Slight A and V periodicity of opposite sign. |
| (5.55) .. | 105.0 while slow | 38.2 | .. | Same. End of exp. |
| 26 .. | 157.5 | 48.7 | Slower than V | Regular. |
| .. | 49.5 while slow | 49.5 | Slow | After rest of ½ hour; sleepy. Marked periodicity of A. |
| 27 .. | 129.7 | 46.5 | Synchron. with V | Slight periodicity. |
| 28 .. | 132.0 | 47.2 | Slow | |
| 29 .. | 140.1 | 42.0 | .. | |
| June 30 to Sept. 16 | — | 40.0-54.0 | — | Pulse taken by attendant. |
| Sept. 21 .. | 131.2 | 27.0 | .. | V slightly irregular. Some periodicity of A. |
| Dec. 17 .. | 99.7 | 39.7 | Slow | At places slight periodicity of A. |
| 24 .. | 106.5 | 48.0 | .. | Regular. |

| DATE. | | A RATE. PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|-------|---|------------------------|-----------------------|---------------------|-------------|
| Jan. | 2 | 109.3 | 32.2 | Synchron. with V | Regular. |
| | 3 | 125.2 | 50.2 | — | " |
| | 9 | 124.5 | 42.7 | Slow | " |
| Feb. | 9 | — | — | — | Found dead. |

Autopsy.—The dog has a very large amount of adipose tissue. The pleura is normal everywhere, excepting adhesions of cardiac surface of right lung to the pericardium. The lungs are everywhere crepitant and only a small amount of frothy fluid exudes from the cut surface.

The two layers of the pericardium adhere everywhere, but they can be separated, except in the field of the operation.

In the heart scars were found having the position and form shown in the accompanying sketch (Fig. 23).

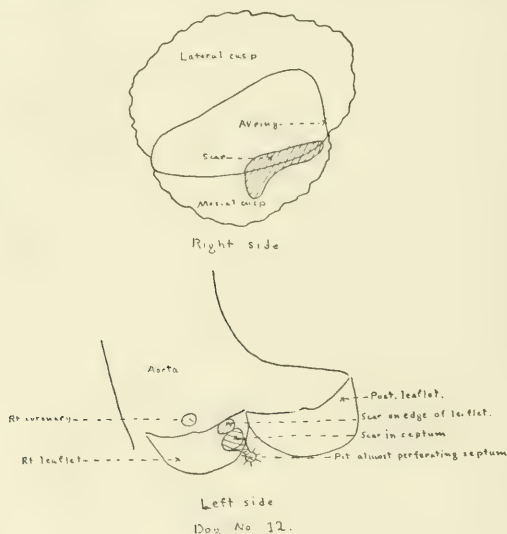


Fig. 23.

Dog No. 13.—Large hound. Operation 4th April, 1907. Block produced upon second trial. Five minutes later, while the block was still complete, the clamp was reinserted and tissue in its grasp thoroughly crushed. Operation completed at 6.10 p.m.

| DATE. | A RATE PER MINUTE. | PULSE PER MINUTE. | RESP. | REMARKS. |
|-------------------|-----------------------|----------------------|-------|---|
| April 4 (10 p.m.) | — | 48 | — | Doing very well. Regular. |
| 5 (10 a.m.) | — | 48 | — | " " " |
| (4 p.m.) | — | 50 | — | " " " |
| 6 | — | 50 | — | " " " |
| 7 | — | 54 | — | " " " |
| 8 | — | 46 | — | " " " |
| 9 | — | 48 | — | Regular. Perfectly comfortable and happy. |
| 10 | — | 48 | — | Regular. |
| 11 | — | 46 | — | " |

| DATE. | | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|-------------|----|-----------------------|-----------------------|---------------------|---|
| April 12 | .. | 165-0 | 39-4 | — | First dressing. All stitches removed. Cardio-grams made. Regular. Block complete. |
| 13 | .. | 165-0 | 46-9 | — | Regular. Block complete. |
| 14 | .. | 150-0 | 46-9 | — | |
| 15 | .. | 142-5 | 45-0 | Rapid | |
| 16 | .. | 150-0 | 42-0 | Synchron. with V | |
| 17 | .. | 127-5 | 40-0 | — | |
| 18 | .. | 142-5 | 43-7 | — | |
| 19-24 | .. | 128-0-154-0 | 40-0-47-0 | — | |
| 25 | .. | 101-2 | 42-0 | — | |
| 26-May 2 | .. | 120-0-131-0 | 37-5-42-7 | Occas. synchn. | |
| May 3 | .. | 108-7 | 39-7 | — | A slightly periodic. |
| 4 | .. | 127-5 | 43-7 | — | Regular. Block complete. |
| 5-10 | .. | 131-0-150-0 | 39-0-43-5 | Occas. synchn. | |
| 11 | .. | 120-0 | 42-0 | .. | |
| 12 | .. | 150-0 | 43-5 | .. | |
| 13 | .. | 120-0 | 40-5 | .. | |
| 14 | .. | 120-0 | 43-5 | — | |
| 15 | .. | 127-5 | 42-0 | — | |
| 16 | .. | 150-0 | 39-0 | — | A slightly periodic. |
| 17 | .. | 112-5 | 39-0 | — | Regular. Block complete. |
| 18 | .. | 105-0 | 36-0 | — | |
| 19 | .. | 127-5 | 39-0 | — | |
| 20 | .. | 135-0 | 36-7 | Occas. synchn. | |
| 21 | .. | 116-2 | 36-7 | — | A slightly periodic. |
| 22 | .. | 112-5 | 31-5 | — | Regular. Block complete. |
| 23 | .. | 105-0 | 31-5 | — | A slightly periodic. |
| 24-28 | .. | 112-0-135-0 | 31-5-39-0 | — | Regular. Block complete. |
| 28 | .. | 105-0 | 33-7 | — | After rest. |
| 29-June 1 | .. | 112-0-127-0 | 36-0-43-7 | Occas. synchn. | Regular. Block complete. |
| June 2 | .. | 93-7 | 35-2 | — | |
| 3-6 | .. | 120-0-127-0 | 31-5-39-7 | .. | |
| 7 | .. | 101-2 | 34-5 | — | A slightly periodic. |
| 8 | .. | 131-2 | 39-7 | — | Regular. Block complete. |
| 9 | .. | 108-7 | 33-0 | — | A slightly periodic. |
| 10 | .. | 75-0 | 31-5 | — | Same. |
| 11-16 | .. | 112-5-135-0 | 35-0-46-5 | Occas. synchn. | Regular. Block complete. |
| 18 | .. | — | — | — | Vagus stimulated. |
| 19 | .. | 120-0 | 42-7 | — | Regular. Block complete. |
| 20 | .. | 105-0 | 35-2 | — | A decidedly periodic. V slightly irregular. |
| 21 | .. | Very slow | 32-2 | — | Marked periodic variations in A make it impossible to estimate rate. |
| 22 | .. | .. | 31-5 | — | Same. |
| 23 | .. | .. | 37-5 | — | Same, but not so marked. |
| 24 | .. | .. | 30-0 | — | Same, but more marked. |
| 25 | .. | 108-0 | 30-0 | — | Regular. Block complete. |
| | | | | | Later, while animal sleeps, same as above. |
| 26 | .. | 114-9 | 43-0 | — | Regular. Block complete. |
| 27 | .. | 106-5 | 41-2 | — | |
| 28 | .. | 90-0 | 40-5 | — | A slow over long periods. |
| 29 | .. | 129-0 | 43-0 | — | Regular. Block complete. |
| 30-Sept. 16 | .. | — | 40-0-56-0 | — | Pulse counted by attendant. |
| Sept. 21 | .. | 102-7 | 39-0 | Slow | Regular. Block complete. |
| | | 37-5 (?) | 37-5 | — | Later, marked periodicity of A. |
| Dec. 14 | .. | 1-0 (?) | 39-0 | Slow | No A waves over long stretches of record. |
| 17 | .. | 105-0 | 42-7 | — | A slightly periodic. |
| 19 | .. | — | — | — | About same as Dec. 14. |

| DATE. | | A RATE PER MINUTE. | V RATE PER MINUTE. | RESP. | REMARKS. |
|---------|----|-----------------------|-----------------------|-------|---|
| Jan. 2 | .. | — | — | — | About same as Dec. 14. |
| 3 | .. | 120.0 | 41.2 | Slow | Regular. Block complete. |
| Feb. 12 | .. | 142.5 | 38.2 | — | Regular at first. |
| 14 | .. | 97.5 | 42.0 | — | Well-marked A periodicity. |
| 18 | .. | 139.5 | 45.0 | — | Slight A periodicity. |
| 21 | .. | 97.5 | 42.0 | — | Some A periodicity. |
| March 6 | .. | 86.2 | 36.0 | — | Some A periodicity. |
| 10 | .. | 114.9 | 38.0 | — | At end of long record some A periodicity. |
| 13 | . | — | — | — | Final experiment. See p. 206. |

Autopsy.—The right lung is firmly adherent to the pericardium. Layers of the pericardium are adherent everywhere, but can be easily separated, excepting over the auricles. The heart weighs 200 gm. The accompanying sketch (Fig. 24) shows the lesions in the heart as determined by vision aided by touch.

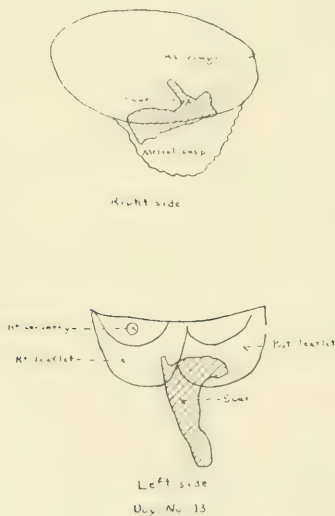


Fig. 24.

BIBLIOGRAPHY.

- ¹ DAWSON. Amer. Journ. of Physiol., 1906, xv, 244.
- ² ERLANGER. Journ. of Exper. Med., 1905, vii, 676; and 1906, viii, 8.
- ³ ERLANGER. Johns Hopkins Hosp. Bull., 1905, xvi, 234.
- ⁴ ERLANGER, BLACKMAN, and CULLEN. Amer. Journ. of Physiol., 1908, xxi, xviii.
- ⁵ ERLANGER. Zentralb. f. Physiol., 1905, xix, 9.
- ⁶ ERLANGER. Amer. Journ. of Physiol., 1906, xvi, 160.
- ⁷ ERLANGER. Unpublished.
- ⁸ ERLANGER. Archiv f. d. ges. Physiol., 1909, cxxvii, 77.
- ⁹ ERLANGER. Amer. Journ. of Physiol., 1909, xxiv, 375.
- ¹⁰ EYSTER. Journ. of Exper. Med., 1906, viii, 565.
- ¹¹ HAYCRAFT and EDIE. Journ. of Physiol., 1891, xii, 426.
- ¹² HEINEKE, MULLER, and v. HOSSELN. Deutsch. Archiv f. klin. Med., 1908, xiii, 459.
(cited in Journ. Amer. Med. Assoc., 1908, li, 1041; and by Lewis, B.M.J., 1908, ii, 1798).
- ¹³ LANGENDORFF. Archiv f. d. ges. Physiol., 1907, cxxi, 54.
- ¹⁴ PAUKUL. Zeitschr. f. Biol., 1908, li, 177.

BREAST PANG.

By H. WALTER VERDON.

(London.)

DR. X, aged 60 years, doing an extensive practice in a suburb of London, describes his own illness in the following terms :—

On the morning of 7th March, 1908, while reading the daily paper after a breakfast consisting of a rasher of bacon, a few pieces of dried toast and a cupful of coffee, I became conscious of a dull, aching pain at the chest. Afterwards for a few seconds only did my mind continue centred in the news. For the pain, at first felt in the mid line beneath the upper part of the sternum, was now extending upwards to the throat, finally to reach the molar region of the jaws, backwards towards the scapulæ and laterally to the axillæ, elbows and wrists. Moreover every moment it was increasing in intensity.

The most extreme manifestation was focused, and could be located, with some degree of exactitude, in the region lying behind the *manubrio-gludiolar synchondrosis*, while painful sensations of lesser magnitude continually radiated from this centre towards the back, neck and arms. Pain did not extend below the plane of the diaphragm, neither was it accompanied by faintness, sickness, or embarrassment of breathing. The pulse was irregular, its rate was rapid enough to be beyond my powers of computation. The radial artery, usually full and strong, felt small and thread-like. The skin was wet with perspiration.

It is said that persons stricken by angina pectoris are distressed with forebodings of impending death. I am not conscious of having entertained any apprehensions of this character. My mind was clear and capable of concentrated thought. I considered the situation for a few seconds in expectation that the symptoms would pass off, but the pain gathering strength rather than abating, I determined that something must be done quickly to obtain relief from my intolerable sufferings. At length I wrote a prescription for nitrite of amyl and sent it by messenger to a neighbouring chemist.

The effort attendant upon this action greatly aggravated my sufferings. Neck and molar pain was intensified. Vision became affected. Objects seen at a distance across the room seemed to stand in a dark field surrounded by mist which rolled in eddies from centre towards circumference.

I had been in extreme pain for twenty-five minutes when the messenger returned, bringing with him a supply of nitrite of amyl capsules. Taking one

I crushed it and inhaled the vapour. Immediately I felt relief, which first reached the jaws, neck and arms, and afterwards the chest. A sore feeling still remained in the substernal region which afterwards was removed by inhalation of fumes from a second capsule. Fifteen minutes later I was attending to the requirements of patients waiting to see me, and except for some shakiness of the limbs feeling no worse for my recent experiences.

A second attack came on a few days afterwards in the early morning. Pain in the substernal region awoke me from sleep and after the lapse of a few minutes involved the whole chest, the neck and the arms. The pain was of the same character as that of the previous attack and as rapidly left me after I had inhaled a few breaths of nitrite of amyl.

Including in the count, seizures already described, I have suffered from five definite anginal attacks, all of which occurred during the months of March, April and May, 1908.

For fifteen months before the date of the first attack of this series I had found myself unable to walk far on rising ground without feeling discomfort and pain in the upper part of the chest which seemed to be associated always in some manner or other with disorders of the stomach and the presence of gastric flatus. Pain was a new condition superimposed upon the symptoms of acid dyspepsia which had troubled me for years. This conclusion is drawn because the breast pang made itself felt sooner after a full meal than after a spare one. More frequently after tea in quantity, sweet cakes and jam, or after soup, vegetables, pastry and milk puddings than after a plain dish such as a grilled chop with no accessories. Moreover, it asserted itself with marked violence when effervescing wines, malted liquors, or non-alcoholic sweet beverages had been drunk with the meal. Pain usually abated or came to an end when exercise was discontinued or when flatus was expelled. After several breaks in the journey and when gastric distension had been relieved by repeated eructations of flatus a considerable length of road might be traversed without the occurrence of any further manifestation of thoracic discomfort.

The pain induced by walking exercise is precisely of the same character as that experienced in the definite anginal attacks of March, April and May, 1908, except in degree and in the extent of area involved. It commences in the substernal region and extends to the inner aspect of the arms as far down as the elbows. It seldom reaches backwards to the scapulae or affects the jaws or neck. When exercise is persisted in it is exaggerated. Upon discontinuance of muscular effort it is relieved. Abatement follows eructation of flatus, inhalation of nitrite of amyl or the exhibition of nitroglycerine.

On some few occasions when, notwithstanding the urgency of my symptoms, I had persisted in going forward to reach my destination without any further halts, the pain in the chest became intolerable, it extended to

the jaws and wrists and began to assume all the characteristics of the anginal seizures already described.

Blood pressure was frequently estimated in the latter months of 1907. It was generally found in the neighbourhood of 165 mm. Hg.. Sometimes it was noticed to fall as low as 120 mm. and on a few occasions it ranged over 200 mm. Both high and low levels were ephemeral, the former corresponding with periods of muscular effort and gastric disturbance.

On 20th November, 1907, on account of the continual findings of high blood pressure, the consumption of animal food was reduced to small proportions. I lived chiefly for some months afterwards upon milk, eggs vegetables, fruit and bread. On the date when this dietary was entered upon I weighed 14 stone 4 lbs. The regime with occasional variations was followed until the 23rd August, 1908. Weight had gradually increased after the abandonment of meat food and now reached 16 stone 2 lbs. Girth at the umbilical plane had increased from 42 inches to 54 inches. Instead of a collar of 16½ inches in circumference I found it necessary to wear one of 18½ inches and this was none too easy of fit.

Blood pressure during the regime fell from 165 mm. Hg. to 145 mm. but when taking exercise I was subject still to ephemeral elevations of abnormally high range. Incidences of thoracic pain were excited more frequently than before and came into evidence before I had walked more than 20 or 30 yards. The dosage of nitroglycerine had been increased from one-hundredth to one-fiftieth of a grain and sometimes two or more tablets were necessary to stave off an impending attack. Moreover during the period of abstinence from meat, namely, in March, April and May, 1908, I had suffered from the series of definite anginal attacks to which reference has already been made.

On the 23rd August, 1908, the "milk-egg-vegetable" regime was abandoned and an "all meat" dietary adopted in its stead. This consisted of a category from which starch and sugar bearing foods were mostly eliminated. Vegetables, fruits, bread, milk, sugars, pastry, wines and fermented liquors were for the most part excluded. The day's rations were selected from a menu containing meat, poultry, game, fish, bacon and cheese, and to these articles were added a few slips of crisp dried toast with an occasional tomato, orange, lemon or dish of spinach. The beverages taken with meals were weak tea, lemon water or whiskey freely diluted with Malvern, Seltzer or Apollinaris water.

Ten days after the adoption of this regime I noticed a remarkable improvement in my general health. I had lost between eight and nine pounds in weight. Flatulence ceased to be a prominent symptom. Incidences of thoracic pain were less frequent. I found myself able to walk 150 or 200 yards without discomfort. Moreover blood pressure had fallen 10 mm. Hg. and ephemeral elevations during exercise did not exceed 170 mm. Hg..

Decline in weight under the "all meat" dietary is illustrated in the figures of the following table :—

| 1908. | | st. | lbs. | | | st. | lbs. | | | st. | lbs. |
|--------|------|-----|------------------|-------|------|-----|------------------|-------|------|-----|-----------------|
| August | 23rd | 16 | 2 | Sept. | 6th | 15 | 4 $\frac{3}{4}$ | Sept. | 19th | 14 | 11 |
| .. | 24th | 16 | 1 | .. | 7th | 15 | 3 $\frac{3}{8}$ | .. | 20th | 14 | 10 |
| .. | 25th | 16 | 0 $\frac{1}{4}$ | .. | 8th | 15 | 2 $\frac{1}{8}$ | .. | 21st | 14 | 9 $\frac{1}{2}$ |
| .. | 26th | 15 | 13 $\frac{3}{8}$ | .. | 9th | 15 | 1 $\frac{3}{8}$ | .. | 22nd | 14 | 8 $\frac{1}{4}$ |
| .. | 27th | 15 | 11 $\frac{3}{4}$ | .. | 10th | 15 | 1 $\frac{1}{2}$ | .. | 23rd | 14 | 8 $\frac{1}{4}$ |
| .. | 28th | 15 | 10 $\frac{1}{4}$ | .. | 11th | 15 | 1 | .. | 25th | 14 | 7 $\frac{1}{4}$ |
| .. | 29th | 15 | 9 | .. | 12th | 15 | 0 $\frac{3}{8}$ | .. | 26th | 14 | 7 $\frac{1}{8}$ |
| .. | 30th | 15 | 8 $\frac{3}{8}$ | .. | 13th | 14 | 13 | .. | 27th | 14 | 7 |
| .. | 31st | 15 | 8 $\frac{1}{4}$ | .. | 14th | 14 | 13 | .. | 28th | 14 | 7 $\frac{1}{8}$ |
| Sept. | 1st | 15 | 8 | .. | 16th | 14 | 13 $\frac{1}{2}$ | .. | 29th | 14 | 6 $\frac{3}{8}$ |
| .. | 2nd | 15 | 7 $\frac{1}{8}$ | .. | 17th | 14 | 12 $\frac{1}{8}$ | .. | 30th | 14 | 5 $\frac{1}{4}$ |
| .. | 3rd | 15 | 5 $\frac{1}{4}$ | .. | 18th | 14 | 11 $\frac{3}{4}$ | Oct. | 2nd | 14 | 4 $\frac{3}{8}$ |

On the 22nd October, 1908, my weight having fallen to 14 stone 1 lb. I found myself able to walk a distance of two miles without pain. On the 1st November I weighed 14 stone 2 $\frac{1}{4}$ lbs. : on the 1st December 13 stone 12 $\frac{1}{4}$ lbs. ; on the 1st January, 1909, 13 stone 11 $\frac{1}{8}$ lbs. The lowest weight reached under the all meat regime was on the 2nd May, 1909, when it had declined to 13 stone 6 $\frac{1}{8}$ lbs.

After this date severe restrictions upon dietary were suspended and excluded articles were admitted in sparing quantities. Blood pressure now registers 130 mm. Hg.. Ephemeral elevations during exercise range within normal limits. Since the abandonment of the milk, egg, vegetable regime waist girth has decreased by 13 inches and collar measurement by 2 inches.

Even now discomfort is sometimes felt in the thoracic region, but its visitations are infrequent. When making a temporary sojourn in the bracing air of the east coast I have found myself able to walk a distance of 7 or 8 miles without experiencing any pain. Sometimes when walking in London I feel discomfort not amounting to pain. Resort to the nitrites is not now necessary, for when perchance a premonitory symptom does make its appearance a halt of a few minutes' duration determines relief.

The specific gravity of the urine is 1024 with an acid reaction. The presence of phosphates is variable. The colour is dark straw. Deposits of a brick dust character not infrequently stain the utensil. Sugar and albumen are absent.

Constipation is the ordinary habit, but it is less marked during the "all meat" regime than during the "milk, egg, vegetable" period.

The heart sounds are normal. The skin inclines to the sallow type. The whites of the eyes have lost their blue tint and assume a dirty yellow shade lasting twenty-four hours or more after the ingestion of sweet foods and fermented beverages.

The chronic acid dyspepsia from which I had suffered for many years is a form associated with the intake of starch and sugar bearing foods. It is excited by bread, milk, cakes, pastry, jams, potatoes and fruits. It is encouraged by wines and fermented liquors, and it is accompanied by the formation of large volumes of gastric flatus. The effect of the ingestion of any of these articles in quantity is generally noticed one or one and a half hours after a meal. The stomach becomes greatly dilated and the discomfort of the distension is aggravated by the constrictions of trouser band or waist-coat. Tension is relieved by the expulsion of flatus. Gastric pain is entirely absent.

The stomach has been always tolerant of meat. Beef, mutton, lamb or pork, fresh or salted, roast or boiled, chickens, game or fish, crabs and lobsters. So strong is the stomach in the digestion of meats of all sorts that even when swallowed in unmasticated lumps they do not provoke discomfort. Indeed, in the absence of starches and sugars the digestive apparatus might be properly described as vigorous.

Relief from attacks of indigestion of this sort is not difficult of attainment. Administration of alkalies when symptoms begin to assert themselves is generally effective for this purpose. A draught of Vichy or Seltzer water, followed by bismuth and iodide of potassium usually causes eructation of flatus and puts an end to gastric discomfort.

In the early months of 1908, before the incidence of any definite attack of angina, I had practised total abstinence from alcohol and tobacco for a period of five weeks. I am not aware that any beneficial results followed. Indeed, at this time attacks of thoracic pain were daily becoming more frequent. Increased frequency, however, may have been due to the "milk, egg, vegetable dietary" which I was following then, and to the gaseous distension of the gastro-intestinal tract which accompanied the observance of this regime.

THE SUCCESSION OF EVENTS IN THE CONTRACTING VENTRICLE AS SHOWN BY ELECTROMETER RECORDS --(TORTOISE AND RABBIT).

BY FRANCIS GOTCH.

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IN a communication to the proceedings of the Royal Society I brought forward the result of an investigation by means of the capillary electrometer upon the course of the contraction wave in the ventricle of the frog's heart when contracting normally in situ¹. The character of the electrometer records appeared to show that "in the natural beat the whole base does not pass simultaneously into the active state with its associated relative negativity, the manifestation of such activity in the part near the exit of the aorta being always delayed."

An extension of the same investigation to the heart of the tortoise, whilst beating in situ, afforded results which led to the same conclusion, and a short notice of this part of the research appeared in the account of the communications made to the International Physiological Congress at the Heidelberg meeting¹. I have since extended the method to the heart of the rabbit, and the results thus obtained form the chief part of the present paper, but it seemed desirable also to place on record the main features of the records furnished by the tortoise heart, more especially as the study of these records, whilst corroborating in their general character those referred to above as to the contraction of the frog's ventricle, raises several points of interest which bear upon the more complex conditions of the mammalian ventricle.

THE TORTOISE HEART.

The investigation of the contraction of the ventricle of the tortoise heart by means of capillary electrometer records was first made by Burdon-Sanderson and Page² in 1883 : the results showed that the excitatory change, when evoked by an artificial stimulus, was propagated from any point of excitation over the muscular fibres of the ventricle. Thus, with two contacts upon the ventricular surface, one near and one more distant from the seat of excitation, records were obtained of the following character : the proximal or near contact was the seat of a sudden electromotive change rapidly cut short, and thus giving, as a record, a spike or initial effect, this was succeeded

by an iso-electrical period terminating in a marked but less rapid electromotive change of opposite sign to the initial one. It is well known that this is the character of the so-called diphasic total effect. An effect of this type signifies (1) the development of activity with its associated electromotive change under the proximal contact, whilst the rest of the tissue is quiescent, thus causing the abrupt initial displacement of the electrometer meniscus; (2) the development of similar activity under the distal contact when the active state has by propagation reached this part of the ventricular substance, thus equalising the whole electromotive difference between the two contacts and bringing back the displaced meniscus, so that the record of (1) with (2) is a spike; (3) a period during which the tissue under both contacts is in a prolonged state of similar activity, and the contacts are thus equipotential as regards electromotive condition; (4) the subsidence of the activity at the contact under which it first began whilst the tissue under the more distant contact, having passed into activity later, still remains in the active state, thus causing again an electromotive difference which must be relatively of opposite sign to the initial effect. Diphasic records similar to the above were obtained by Burdon-Sanderson in the excised tortoise heart whilst beating normally, the contacts in this case being at the base of the ventricle and at the apex respectively. Hence the wave of activity in the tortoise heart during the natural beat has been generally described as commencing at the base and passing along the heart substance to the apex.

It appears probable from the records now to be described that the natural course of the propagated activity in the tortoise ventricle is of a more complex character. It probably follows a number of routes, but all these seem to have one element in common: they all start from the part of the ventricle base which is in structural connection with the two auricles, and all terminate, after proceeding towards or to the apex, in a part of the base which is in structural connection with the issuing aorta.

The experimental data on which this conclusion is based are derived from the study of the electromotive potential differences observed when two contacts are placed on various points of the surface of the ventricle beating in situ and not excised. The potential differences are themselves inferred from the photographed records of the movements of the mercurial meniscus of a highly sensitive capillary electrometer, the image of which, appropriately magnified, is projected upon the surface of a photographic plate travelling at a uniform and known rate.

In order that the heart should be as little disturbed as possible the preparation was made in the following manner.

The brain of the tortoise (*Testudo graeca*) having been destroyed, the ventral carapace was perforated by means of a large trephine or otherwise, and the opening then suitably enlarged so as to expose the heart in situ. All bleeding points were, as far as possible, plugged or ligatured; the pericardium was carefully opened and the contacts then made with the

electrometer by means of special nonpolarisable electrodes carrying long flexible threads the ends of which could be placed on any desired point of the cardiac surface. In order to reach the edges and dorsal part of the ventricle, the apex was carefully lifted and held up. It was ascertained by observation that the circulation was still going on fairly well, the heart filling with blood at each diastole.

Contacts upon entrance of veins into auricle and upon the ventricle apex respectively.

By this arrangement both the auricular and ventricular masses lie between the two contacts so that the activities of both chambers can affect the recording instrument. An example of the records of the electrometer movements is shown in Fig. 1. The curve is to be read from left to right, and the time tracing above the record indicates $\frac{1}{2}$ sec. for each full vibration; this holds good for all the figures given in the present paper.

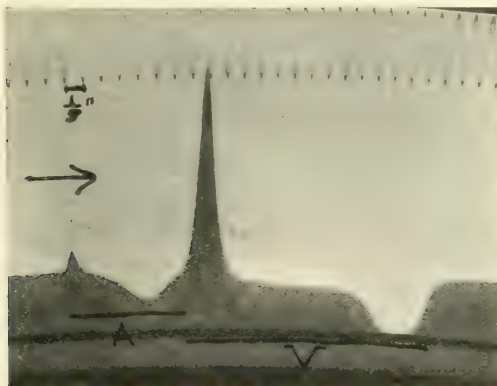


Fig. 1. Electrometer record with the contacts upon the sinus and the ventricle apex respectively. Upward movement signifies relative negativity of the sinus contact (tortoise heart). One beat only is shown in the record.

It will be observed that there are two sets of diphasic effects, one preceding the other above the base lines marked respectively A and V. The first (above the line A) is the total auricular change between the contacts, the second (above the line V) is the ventricular change.

Several points are significant in this and similar records. In the first place it appears that with this disposition of contacts, the whole ventricular mass when quiescent forms an indifferent conductor to the active auricle, whilst the auricle in its turn when quiescent forms an indifferent conductor to the base of the active ventricle.

In the second place the strictly diphasic character of the auricular effect shows that the activity commencing near the veins is propagated to the auriculo-ventricular groove, whilst the strictly diphasic character of the ventricular effect shows that the ventricular activity is propagated from the groove to the apex after the auricular propagation has ceased. In the third place such a record furnishes data for the estimation of the rate of propagation in the auricular and ventricular substance respectively. The time interval between the commencement and the summit of the first small spike must represent the time elapsing between the commencement of the auricular activity near the veins and its arrival at the auriculo-ventricular groove. This time in the record shown amounted to 0.08 sec., and since the measured length of the tissue was 1 cm., the rate of propagation would be 120 mm. in 1 sec.. On the other hand the time interval between the commencement and the summit of the large ventricular spike represents the time elapsing between the commencement of the ventricular base activity and the occurrence of such activity beneath the apex contact. This time is 0.35 sec., and since the measured length of intervening ventricular tissue was in this case 3 cm., the rate of propagation was 90 mm. in 1 sec.. In the particular instance shown the temperature was 12° C., the rate being much accelerated by rise and slowed by fall of temperature. Records obtained in a similar way from other specimens gave very similar results, the auricular propagation rate varying between 110 and 140 mm. per second, the ventricular propagation rate between 75 and 100 mm. per second. It would seem, therefore, that in the tortoise heart, although the propagation is of the same general order in both muscular substances, it is quicker in the auricular than in the ventricular muscle.

Finally, as regards the total time of the electrical responses, the curves need appropriate analysis, but this much may be inferred from the particular record shown in Fig. 1; the auricular total effect lasts about 1 sec., whilst the total ventricular effect, including both base and apex, lasts 3½ sec..

Contacts on ventricle, viz., one on the external border near base, the other on the apex.

With this disposition of contacts records were obtained which are analogous to the second or ventricular part of that just shown in Fig. 2. An example is displayed in Fig. 2. It is obviously a strictly diphasic curve with an initial tall spike followed by an equipotential period and terminating in a phase of opposite sign to the initial one. It thus shows that the wave of

activity with its associated electromotive state (relative negativity) is propagated beneath the contacts from the base to the apex at a rate of the order already indicated.

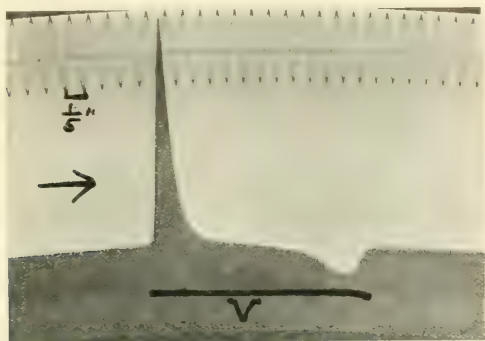


Fig. 2. Electrometer record with one contact on the lateral border of the ventricle, and the other contact on the apex (tortoise heart). One beat only is shown in the record.

Contacts on ventricle, viz., one lying near the aorta, the other on the apex.

If the ventricle apex contact is kept undisturbed, but the base contact is shifted so that, instead of merely touching the external border of the ventricle, it lies along a large portion of the base including the part from which the aorta springs, then the whole character of the electrometer record is changed.

It is now of the type shown in Fig. 3. It will be observed that commencing on the left hand, two slight downward movements are seen above the line marked A; these correspond in time with the commencement and end of the auricular contraction, and serve to show its presence; their interpretation is complicated and needs further special investigation. This is succeeded by a large ventricular change above the black line marked V. The curve is one in which the initial rise occurs as before, but instead of being brought back to the base line by a subsequent sharp fall, it is only partially brought back and after a wavy course again rises as a terminal phase, the whole then subsiding to the true base line. The complexity of this curve indicates that the whole base process, whose relative negativity during the active state undoubtedly causes any rise in the record, lasts longer than the apex process. The duration of the apex process may be approximately realised by that of the valley in the curve commencing at the summit of the spike. That this is the true interpretation of the curve is abundantly shown

on comparing it with the numerous records, described by Burdon-Sanderson and others, in which local warming of the apex, and thus acceleration of its activity, produces curves of the same type.

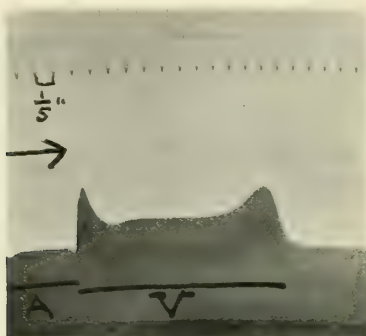


Fig. 3. Electrometer record obtained from the tortoise ventricle beating in situ, with one contact lying across the base so as to touch the aortic part, the other on the apex. Upward movement signifies relative negativity of the base contact. One beat only is shown on the record.

The curve has other points of interest. It displays features which are seen in records obtained from the mammalian heart which will be referred to later. But as regards its main characteristic, namely the terminal phase, a peculiar significance lies in the circumstance that it is the normal record of the heart when beating in situ if one contact is extended so as to embrace a large part of the auriculo-ventricular groove, whilst the other lies on the apex only. It is clear, on comparing Fig. 3 with Fig. 2, that the special condition of the base which causes this to show such prolonged activity may be related to that portion of the mass of muscular substance situated near the aorta.

In order to determine this the base contact was arranged so that it could be carefully shifted along the groove from one spot to another.

Contacts on ventricle, viz., one touching the groove at various definite points, the other on the apex.

(1) If the base contact is arranged just to touch the border of the groove as far as possible from the exit of the aorta, whilst the remaining contact lies on the apex, then the records all have the character shown in Fig. 2, that is simple diphasic effects, or, to use the nomenclature first suggested by Waller, effects of the base apex (b, a) type.

(2) If the base contact is moved along the groove so as to touch a part lying nearer to the exit of the aorta, whilst the remaining contact remains as before on the apex, then the records have the character shown in Fig. 4. This resembles the simpler diphasic curve of Fig. 2, but differs from it in one significant point since it shows a final rise at the end in the same direction as the initial one or spike. It is clear that this final rise must be the residue of activity near the base which alone can cause a change of this electrical sign. Hence, the type of effect is now base apex base (b, a, b).

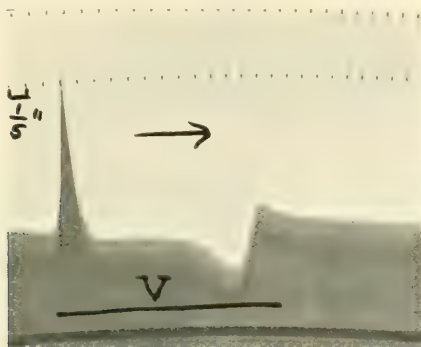


Fig. 4. Electrometer record when two contacts are placed upon the ventricle of the tortoise beating *in situ*, one of these being on the base about half way between the exit of the aorta and the lateral border, the other on the apex. Upward movement signifies relative negativity (activity) near the base contact. Only one beat is shown on the record.

(3) If the base contact is shifted so as to lie quite close to the part of the ventricle from which the aorta springs, whilst the other contact is still left upon the apex, then the records are similar in character to that shown in Fig. 3, i.e., of the type (b, a, b), the final base effect being accentuated.

It appears to follow from the above considerations that the ventricular base is the seat of two active changes which occur at two different periods of time, one immediate, the other delayed, and that whilst the immediate active effect is alone present in such base tissue of the groove as borders on the auricles, the delayed active effect is present in the ventricular tissue leading to the aorta.

The active process thus appears to pass as a wave from the auriculo-ventricular junction along the ventricular substance towards the apex, but returns to the neighbourhood of the aorta, the last part of the ventricle to commence contracting being that which lies near the exit of the aorta. Thus, the ventricle still bears the impress of its embryonic tubular formation.

Both contacts on the ventricular base, one on the free border, the other near the aortic exit.

If the view just enunciated is correct, it ought to follow that when one contact is placed on the base far from the aorta (the lateral border), and the other on the base close to the aorta, some of the records should show a succession of events of the diphasic type, for the base contraction in these two regions cannot be simultaneous. The base border contact should show initial relative negativity since this is in complete connection with the seat of the immediate activity; this would then be cut short when the delayed activity around the spring of the aorta occurred, and since such delayed activity must outlast the earlier immediate activity, there should be a terminal phase of opposite sign to the initial one. The records are likely to be complicated by the contraction of adjoining and intervening parts, but it was

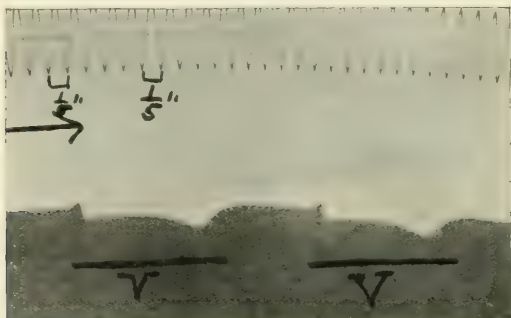


Fig. 5. Electrometer record from the tortoise ventricle beating in situ, when one contact was placed on the lateral border of the ventricle, the other on the ventricle close below the exit of the aorta. Upward movement signifies relative negativity (activity) of the tissue under the border contact. Two beats are shown on the record, each occupying the time from left to right indicated by the black line marked V.

to be expected that a considerable proportion would give clear evidence of uncomplicated diphasic changes. If records of such diphasic effects can be obtained under these circumstances, then strong support is afforded for the view that the aortic base tissue does not pass into activity until some little time after the rest of the ventricle has begun to contract. This was borne out by the actual records for a large proportion of these were of the type shown in Fig. 5, particularly when the border contact was on the right side of the ventricle as far as possible from the spring of the aorta.

Each of the two curves read from left to right displays during the ventricular activity, indicated by the black lines marked V, first a rise cut short by a fall, and at the end a movement in the opposite direction to the initial rise, in short a true diphasic effect. It made no difference as regards the essential character where the first base contact was placed as long as it was near the groove, and the second near the base of the aorta. On the other hand if the first contact was shifted towards the apex most complicated records were obtained as, indeed, might be expected from the number of open routes for propagation which exist across the heart substance. These records need careful analysis before any definite conclusions can be drawn as to such cross routes.

Contacts on the whole of the base, including the aorta, and on the apex after getting up intracardiac pressure.

The physiological meaning of the delayed base activity in the region of the aorta seems sufficiently obvious. It is the final act of the ventricle, and is related to the development of the heart as a tube; moreover, it is of fundamental importance as the final expulsive power in such ventricular tissue as surrounds the cavity leading into the aortic exit. In the frog's ventricle this part has its activity accentuated by rise of aortic blood pressure, and it was to be expected that a similar accentuation might be found in the tortoise. By various procedures, of which constricting the aorta seemed the most suitable, the pressure of blood in the aorta near the heart was raised, and records taken of the ventricular activity under these conditions. As a rule the contacts were placed one across the whole base, and the other on the apex. An example of the type of record now obtained is shown in Fig. 6.

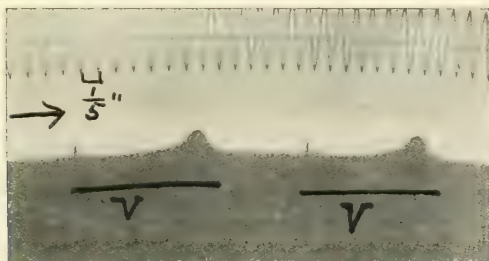


Fig. 6. Electrometer record obtained from the tortoise ventricle beating in situ, when one contact was placed across the base including the aortic exit, the other on the apex. The intracardiac pressure was raised by constricting the aorta, thus distending the ventricle. Two beats are shown on the record at the times indicated by the dark lines.

In the above record the changes are obviously modified. They comprise the following events during ventricular contraction, the duration of which is shown by the line marked V. The initial change is an extremely sharp rise cut short in 0.03 sec. by a change in the opposite direction, this being itself cut short after 0.03 sec. by a change in the same direction as the initial one, the whole then remains balanced, indicating that all parts are in equal activity, until gradually a conspicuous rise in the curve occurs which constitutes the terminal effect. There is thus a double spike, a brief one up and a second brief one down—and this may be interpreted as meaning accelerated propagation from base to apex, and from apex back to aortic base. The rate of propagation would, if this interpretation is correct, appear to be of quite a different order to that indicated in the foregoing records amounting to about 3 metres per second, whether the propagation is from base towards apex or back towards the aortic base. As a result of the rapid propagation, and thus the rapid succession of events, the initial changes are small as regards actual electrometer displacement although of such steepness as to show considerable electromotive potential difference. The conspicuous terminal rise indicates that, whilst all parts of the ventricle share in the general increase of activity, the aortic part is particularly affected, being now of a much more prolonged character, and thus producing a terminal rise indicative of base negativity (i.e., activity) which finally overpowers the activity of all other parts; thus the type is markedly b, a, b.

A special feature of a record such as that in Fig. 6 is its general resemblance to many records of the heart in man. It thus seems extremely improbable that such characters of human electrocardiograms as are also prominent in these tortoise heart records can be in any way associated with the existence in the mammal of two ventricles, even though the activities of these may not be strictly contemporaneous. In this connection it may be remarked that the same degree of resemblance in the electrometer records exists between those obtained from the ventricle of the heart in situ of both the tortoise and the frog on the one hand, and those obtained from such mammals as the rabbit on the other; this will be evident when the latter class of records have been exemplified and described.

THE RABBIT'S HEART.

The electromotive changes in the mammalian heart during activity have been investigated in situ by a large number of observers, the instrument chiefly used for the purpose being the string galvanometer. Yet, as far as I am aware, the particular feature brought out in the present series of records has not been dealt with from the present point of view. This point of view is one which localises at the aorta the presence to an accentuated degree of a ventricular terminal phase by showing that there is always

delayed ventricular activity around the exit of the aorta (or the pulmonary artery).

In order to ascertain the normal succession of electrical events and localise the seat of the activities, of which these events are the signs, it appeared essential that the heart should be exposed so that the position of the contacts upon its surface could be accurately determined. As far as I can ascertain the first investigation of this character upon the exposed mammalian heart beating in situ was carried out by Bayliss and Starling¹.

Using the capillary electrometer on the exposed heart of the cat and dog, these observers found that many records showed peculiar varieties inasmuch as the base effect outlasted the apex effect. They were inclined to attribute this to the parts being unequally cooled by the air entering the lungs or to the apex being more warmed than the base owing to its proximity to the liver, but the foregoing observations on the tortoise, together with those previously published on the frog, show that similar varieties can be observed in cold-blooded animals, hence this explanation is rendered most improbable. It appears now that the phenomenon is characteristic of the activity of the vertebrate heart when appropriately examined in situ.

The method of experiment.

All the records were obtained from the rabbit anaesthetised by the introduction of chloral hydrate (1 gm. per kilo of body weight) into the alimentary canal. Artificial respiration was employed by a tracheal tube, and the thorax then opened by dividing the ribs, care being taken to stop all bleeding points; with this object ligatures were passed around the sternum before this was divided and partially excised. In the earlier experiments the pericardium was freely opened immediately, but in later ones it was opened when and where it was found necessary for the introduction of the electrode contacts. The electrodes consisted of a slight modification of the usual nonpolarisable form; each carried a long bundle of threads plastered with kaolin and kept moist by saline, this was drawn through a very flexible fine india rubber tube, 6 to 8 cm. long, which was lightly held in a special adjustable stand. It was ascertained that by means of these flexible tube electrodes a contact could be made with the deeper parts of the heart without any risk of disturbance of an electromotive character due to the artificial respiration moving the neighbouring lungs; moreover, the extreme flexibility of the tubes allowed these to sway with the movements of the lungs, etc., without displacing the little brush of saline threads projecting from the end of each tube from the heart surface; these latter remained attached to the point on the heart to which they had been applied all through such movements. This form of electrode proved of great service and permitted an exploration of the heart to be conducted through a comparatively small opening in the thorax.

The contacts were connected to the sensitive and rapidly moving electrometer used by me for other experiments, and described in previous published papers, in the Oxford Laboratory; the mercurial meniscus was, as in all these experiments, suitably magnified and its movements photographed by projection upon a photographic plate travelling at a suitable rate.

In all cases the positions of the contacts were carefully noted and, if necessary, verified by subsequent examination.

Contacts on the base near the groove and on the apex of the ventricle.

(1) *Right side.*—With one contact on the right base near the groove, and the other on the apex, the records obtained were of the character shown in Fig. 7.

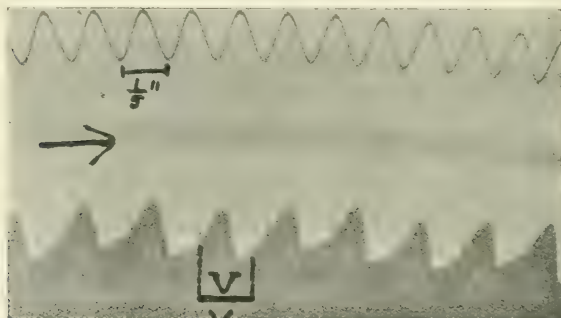


FIG. 7. Electrometer record from a rabbit's heart exposed and beating in situ. Animal under chloral hydrate with artificial respiration. Contacts, one on the right base, the other on the right apex. Eight full beats are shown on the record. The commencement of the beat is on the left hand edge of the dark line, the beat duration is indicated by the length of the dark line. Upward movement signifies relative negativity (activity) of the part at or near the base contact.

The record embraces eight ventricular contractions occurring in about 2 sec., the rate of beat was thus about 240 per minute. Each electrical change during activity (above the black line marked V) consists of (1) a sharp rise, indicating relative negativity (activity) of the base; (2) an equally sharp fall indicating the occurrence of such relative negativity (activity) at the apex; (3) a slower but prominent rise indicating an accentuation or a new development of relative negativity (activity) of the base; (4) a more rapid fall which returns first slowly then quickly until the next repetition of (1). The record thus is of a quadriphasic type, base, apex, base, apex (b, a, b, a).

The time between the commencement and the summit of the sharp rise, constituting the first event, is presumably that which intervenes between the commencement of the activity at the base and the commencement of such activity at the apex, it is thus the time of transmission of the active state from the base to the apex. In this record it amounts to a little less than 0.01 sec., and since the distance between the contacts was 15 mm. the rate of transmission was from $1\frac{1}{2}$ to 2 metres per second.

In other records rates varying between 1 and 3 metres per second were indicated, the former with hearts beating slower at 150 to 180 per minute, the latter with hearts beating faster at 300 per minute.

When the heart was beating at a quite slow rate for the rabbit, 60 to 80 per minute, the rate of transmission indicated by the record was, in some instances, only $\frac{1}{2}$ metre per second.

The above characteristic quadriphasic effect, with its pronounced second accentuation of base negativity overpowered finally by apex negativity, indicates that whilst the whole electromotive change at the base has a marked accentuation, coming on after the apex effect has begun, yet the total change at the apex outlasts that of the base. It has been suggested that there must be peculiarities in the character of the electrocardiograms obtained from the mammalian heart owing to the two chambered ventricle. It, therefore, seemed advisable to duplicate all records by arranging the contacts in similar relative positions on the two sides of the heart. The record just referred to was one of such comparison records and is to be compared with that to be now described.

(2) *Left side*.—In order to get at the left side the flexible tubes were pushed down into appropriate positions. The heart was beating very vigorously, as is shown by its frequency, and the records were of the character displayed in Fig. 8.

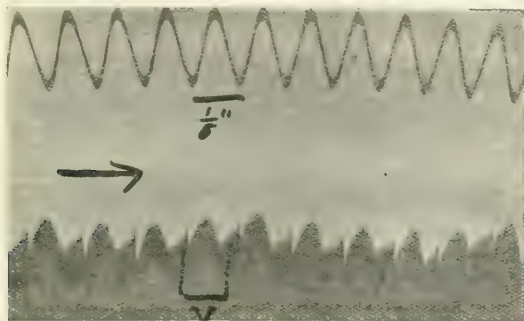


Fig. 8. Electrometer record similar to that of Fig. 7, but obtained by contacts placed on the left base and the left apex of the same animal. Ten beats are shown on the record. The black line marked V indicates the duration of a ventricular contraction.

The record comprises ten completed ventricular contractions in 2 sec., giving a rate of beat of about 300 per minute. Each beat is associated with the following electromotive changes (1) A sharp rise; (2) A conspicuous and rapid fall; (3) A second more prolonged rise; (4) A second more prolonged fall returning at the end of the activity. It thus shows like the right ventricle an effect of the base, apex, base, apex, or quadriphasic type (b, a, b, a). There are some differences between this and the right ventricle record. In the first place the whole effect is smaller, but since the deep tissues, lungs, etc., surround the deep left side of the heart far more than the more superficial right side, this is, in all probability, simply due to short circuiting. A more important feature generally found in my records of the left side is the accentuation of the sharp downward movement, i.e., the second event. This movement, being interpreted as the sign of development of activity under the left apex contact, indicates by its extent that the ratio of apex activity to base activity is greater on the left than on the right side. It is significant that neither in these nor in any of my records is there any indication of a downward movement preceding the sharp rise of the spike: such preceding downward movements only occur in my experience when the base contact is so near the groove as to be affected by the preceding activity of the auricle, or where the whole heart lies between the contacts.

Same contacts, the heart beating more feebly.

In most experiments the force of the heart beat became gradually weakened in the course of a prolonged investigation, and, as this weakening progressed, alterations were always observed in the character of the records. The characteristic feature of these alterations was found to be a diminution

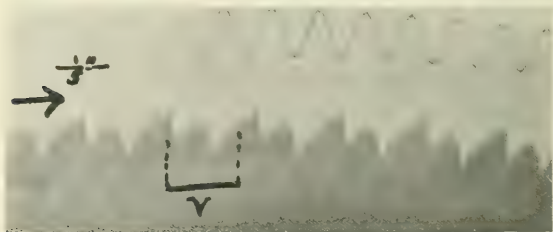


Fig. 9. Electrometer record from a rabbit's heart beating in situ, with one contact on the left base, the other on the left apex. The heart is beginning to beat slowly, 170 per minute instead of 240. Five complete beats are shown on the record. The duration of a ventricular contraction is shown by the black line marked V.

in the amount of the third event, in short the delayed *or* second base activity becomes less conspicuous and as a result the fourth event becomes much more marked. Examples are given in Figs. 9 and 10.

The record in Fig. 9 comprises five to six successive beats with their associated electromotive changes: the rate of beat is slowed to 170 per minute. The record was taken from the left side of the heart, but the right side gave records of similar character.

The movements of the mercurial meniscus during each beat are of the following character if read from left to right above the black line marked V: (1) sudden rise, base activity: (2) sudden more extensive fall, apex activity: (3) a diminished but distinct second rise, indicating further base activity: (4) a pronounced fall from which return is at first more rapid then slow. It thus appears that the apex activity is now, as a whole, much more prominent than the base activity, but that there is still a second base effect which, occurring after the apex activity has commenced, has subsided before such activity is completed: hence the quadriphasic type, base, apex, base, apex, is now very plain.

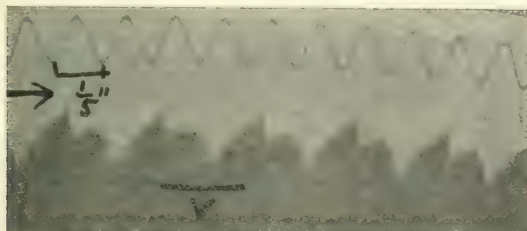


Fig. 10. Curve from a rabbit's heart with the same contacts as in Fig. 9, but with a still slower rate of beat (140 per minute).

As the heart beats subside in force this diminution in the third event becomes more and more marked so that records occur in which its effect is barely perceptible. An example of this is given in Fig. 10 taken from the left side of the heart. It will be observed that each beat is associated with electrometer movements which, read from left to right above the black line marked V, are as follows:—(1) small upward sharp movement (base activity): (2) extensive sudden downward movement (apex activity): (3) slight upward movement soon subsiding: (4) conspicuous downward terminal movement returning at first rapidly then slowly.

I possess a very large number of records of this character: they evidently tend towards the diphasic type, and it is obvious that if event (3) were

altogether removed, the successive changes would be (1) base activity followed by (2) and (4) both of which signify apex activity (i.e., diphasic).

With the base contact across the mass of the ventricle, although my records may approach this diphasic type, none of them actually attain that character some indication of event (3) being perceptible in all.

Thus in the record given in Fig. 11, taken from a feebly beating heart, the apex (downward) effect, although very marked, still shows the presence of a slight later base change as a slight upward rise.

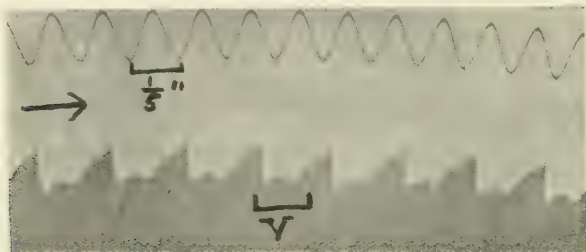


Fig. 11. Electrometer record from a feebly beating heart, with the same contacts as in Figs. 9 and 10. The record of each cardiac change approaches the diphasic (base, apex) type.

Contacts, one near the border of the right ventricle, the other on the apex.

If, in the strongly beating heart, the base contact is shifted towards the border, the other contact remaining on the apex, it very often happened that the record was like that obtained from the feebly beating heart. That is to

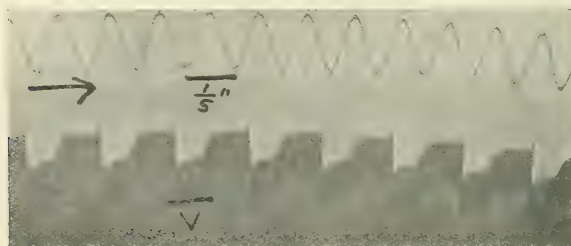


Fig. 12. Electrometer record of a rabbit's ventricle (right side) with one base contact towards the border of the ventricle, the other on the apex. Eight beats are shown on the record. Rate 240 per minute. The black line marked V indicates the duration of contraction in one case. Apex (downward movement) is predominant.

say, of the successive events referred to above, event (3), although present, becomes feeble, whilst events (2) and (4), apex ones, become, therefore, conspicuous. An example of this is given in Fig. 12 which may be compared with Fig. 11.

Contacts, one on the border of the ventricle, the other on the apex.

If the base contact is still further shifted so as to lie on the extreme lateral border of the ventricle some little way from the auriculo-ventricular groove, whilst the other contact remains on the apex, records of a strictly diphasic type were very frequently obtained.

In Fig. 13 such a record is shown. It was taken from the right side of the heart, and includes the changes occurring in nine successive heart beats. Their character is shown in any one of the series. On reading from left to right, above the black line marked V (ventricular contraction), there will be seen (1) the characteristic sharp upward movement indicating the relative negativity (activity) of the muscular substance underneath the lateral

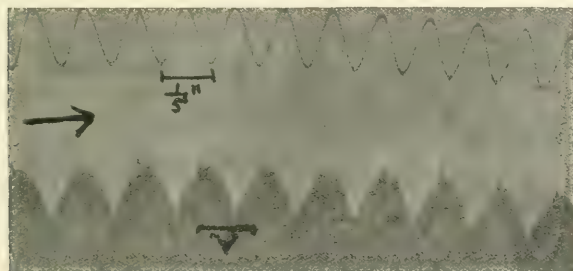


Fig. 13. Electrometer record from the right ventricle of a rabbit, one contact on the lateral border as far as possible from the aortic attachment but near the base, the other on the apex. Nine beats are shown on the record. The rate of beat is 250 per minute. The commencement, duration, and end of the ventricular contraction is indicated by the black line marked V. Upward movement indicates relative negativity (activity) of the border contact.

border of the ventricle ; (2) the sudden downward movement (commencement of apex activity) which reaches a certain point, and is succeeded by (3) a small but distinct iso-electrical period, the meniscus remaining approximately level ; (4) a large sweeping downward movement which culminates and returns first rapidly then more slowly. This corresponds in general character with the diphasic effects obtainable from the ventricle of the frog and the tortoise with similarly placed contacts. It indicates the occurrence of a

propagated wave of activity from the base along the border of the ventricle towards the apex, uncomplicated by other events occurring elsewhere in the ventricular mass.



Fig. 14. Electrometer record under the same conditions as those of Fig. 13, but obtained by contacts on the lateral border and apex of the left ventricle. The rate of beat is 250 per minute.

In Fig. 14 a record of a similar uncomplicated diphasic type is shown, which was obtained by placing the contacts on the lateral border and apex of the left ventricle. The only difference is a diminution in the size of the electrometer excursions due, as previously indicated, to the surrounding tissues short circuiting in greater degree this deeper aspect of the heart. In both cases the heart was beating vigorously at a rate of 250 per minute.

Contacts, one on the aortic part of the base, the other on the left apex.

A great contrast to the preceding records is furnished by those obtained when the base contact is placed close to the ventricular mass from which the aorta springs. In Fig. 15 such a record is shown comprising seven successive heart beats, all of similar character. The black line, marked V, indicates ventricular activity, and above this from left to right are (1) the rise of the spike (general base activity); (2) its sudden considerable fall (apex activity); and (3) a very prominent second rise (base activity), which subsides at first rapidly then more slowly until the next beat, with its associated electrical changes, occurs. This is the triphasic type of total effect, event (4) of the succession described in Figs. 8, 9, etc., being now absent or masked by the great accentuation and duration of its predecessor, event (3). It is clear that the later development of the base activity indicated by the large rise in the curve is so prolonged as to outlast the apex activity indicated by the sharp fall of the curve, for the terminal subsidence is now merely the return of the displaced mercurial meniscus as event (3) passes away.

This is still more strikingly displayed if, by slight compression of the aorta, the resistance to the exit of the blood is increased and the force of the heart beats is thus raised.

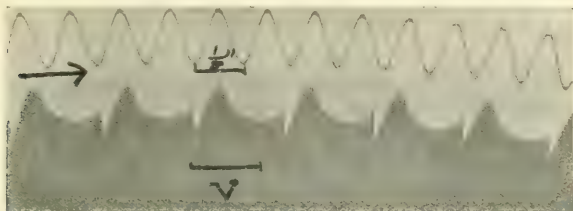


Fig. 15. Electrometer record with contacts placed one on the base close to the aortic exit, the other on the left apex. Upward movement indicates relative negativity (i.e., activity) of the base. Six beats are shown on the record. The commencement, duration, and end of contraction are indicated by the black line marked V.

In Fig. 16 is the record of a series of electrical effects under these circumstances. Beginning with the small upward sharp spike in each case, and reading from left to right over each black line, it will be seen that the second rise, event (3) in the preceding descriptions, becomes more and more marked until, in the third beat of the series, the spike can scarcely be detected over the appropriate black line marked underneath, which indicates the beat. The spike is, however, quite plain on my records although it is indistinct in the reproduction of the record given in Fig. 16. Then follows an effect of the quadriphasic type, with slight final apex or downward movement at its end over the line marked with a cross (X). This is succeeded by another group of triphasic type effects, with increasingly conspicuous second rises in the

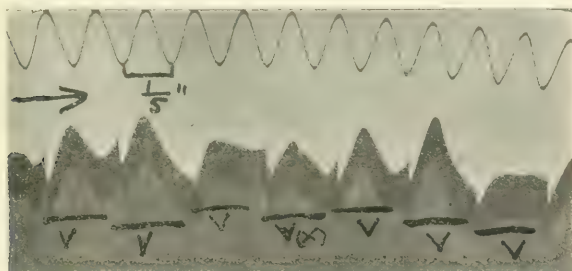


Fig. 16. Electrometer record of a beating ventricle with one contact on the base near the aorta, the other on the left apex. Effect of increased intracardiac tension by constricting the aorta.

two first instances and a prolonged low rise in the third preceded by a spike, indistinct in the reproduction but quite plain in the actual record.

Similar records, though not so marked, were obtained from the right ventricle when the base contact was placed on the part from which the pulmonary artery springs.

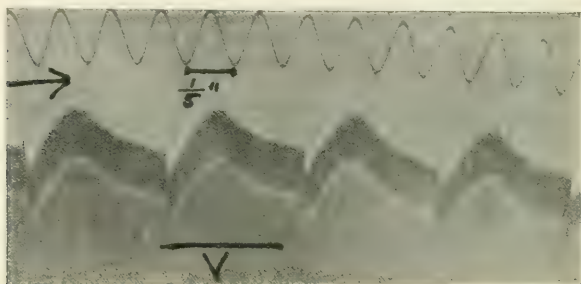


Fig. 17. Electrometer record obtained from the heart of a rabbit with one contact around the aorta as close as possible to the heart, the other on the left apex. Duration of contraction is indicated by the dark line marked V. Four complete beats are shown on the record. The rate of beat is 120 per minute.

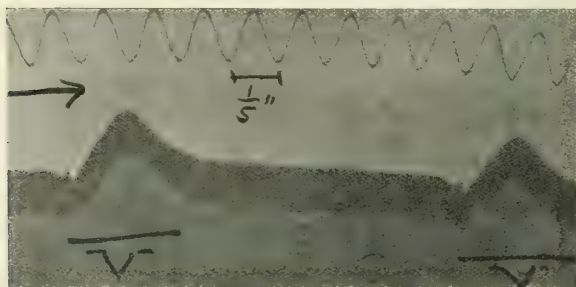


Fig. 18. Similar record with same contacts as Fig. 17, but with the heart beating only 40 times per minute.

When all these results are compared with those records obtained from the frog and tortoise heart which show triphasic effects the meaning of the phenomenon forces itself upon the mind. It is explained by the acceptance of the view that the contraction wave of the ventricle begins generally over the base somewhere near the groove, is then propagated

towards the apex, and returns by cross routes to the aortic exit, hence, this part is the last to develop activity, the part in question being the portion of the base which lies near the aorta on the left side and the pulmonary artery on the right side; further, it would appear that until the arrival of this return wave these portions remain quiescent. The succession of electrical events is thus the sum of the sequence of the activities in three situations, viz., base, apex, base. These activities follow one another in rapid succession, but each has its own period of duration, and it would seem that sometimes the second activity, apex, contraction, is more prolonged than the others, causing quadriphasic records, but that when the part investigated lies very close to the spring of the issuing aorta or the pulmonary artery, then the third activity is overpowering both in amount and duration. Hence, this third activity must be very local in its seat.

In order to test the validity of this explanation records were made under two special conditions as regards the position of the contacts.

(1) The first of these special conditions was the following: One contact was so arranged that it embraced the aorta near its emergence from the heart, whilst the other contact lay upon the left apex. In order to secure the isolation of the looping threads which formed the aortic contact, strips of fine sheet india rubber were employed. The necessary manipulation involved considerable exposure and some displacement of the parts, so that as a rule the heart was obviously affected and the beats were distinctly slowed. It would not, therefore, have been surprising if the presumed aortic base effect had been found to be comparatively inconspicuous, but, as a matter of fact, in these records it was extraordinarily marked, and remained so even when the beats were quite slow, the rate of beat being reduced in one instance to 40 per minute. In Figs. 17 and 18 examples are given of the records obtained under these circumstances.

It will be observed that in both the above records (Figs. 17 and 18) each heart beat, read from left to right, is associated with electromotive changes causing in the record, (1) the sharp small rise (base activity); (2) the pronounced sharp fall (apex activity); and (3) a very marked long rise subsiding slowly. This is even more marked in the heart beating 40 per minute (Fig. 18) than in that beating 120 per minute (Fig. 17). Thus, event (3) is localised, as regards the left side, to the aortic part of the ventricle.

(2) The second of the special conditions was based upon the following considerations. If the base of the ventricle somewhere near the groove is the starting point of the general ventricular activity whilst that near the aorta is the local seat of an activity, delayed because it is the point which the wave of activity (however propagated) reaches last of all, then this should display itself when two contacts are placed upon the ventricle equidistant from the groove, one far away from the aorta, the other near the aorta.

Contacts were, therefore, carefully arranged in this way upon preparations which were solely utilised for this class of experiment. The records

obtained differed as regards their fine details in different preparations, but all showed unmistakably diphasic types of effect, the part away from the aorta becoming first relatively negative to that near the aorta and then relatively positive. In some cases the results were strikingly diphasic, an example of which is shown in Fig. 19.

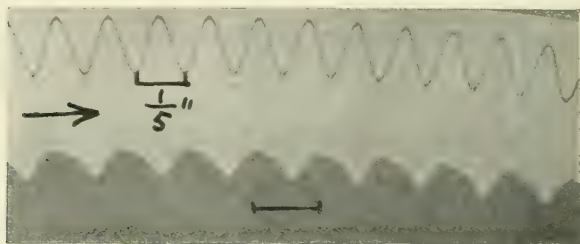


Fig. 19. Electrometer record obtained from the ventricle of a rabbit's heart, with one contact far away from the aorta on the border of the base, the other close to the root of the aorta. Nine beats are shown on the record. The rate of beat is 240 per minute. Upward movement indicates relative negativity (activity) under the border contact. The dark line indicates ventricular contraction.

The record comprises nine beats, the heart beating 240 times per minute. Each beat, marked by the black line, shows (1) a small but distinct sharp rise indicating relative negativity (activity) of the tissue under the contact away from the aorta, (2) its return, followed by a short period of equipotential, (3) a pronounced descent which returns and is followed by the next beat. The pronounced descent is relative positivity of the base away from the aorta, that is, negativity (activity) of that part of the base near the aorta. This must mean (*a*) that the activity of these two parts does not commence simultaneously, that of the portion near the aorta being always delayed, and (*b*) that the change under the portion near the aorta is the most prolonged of the two base activities and remains after that of the other portion of the base has begun to relax.

On all these grounds there is little doubt in my mind of the truth of the remark made by Nicolai in reference to the terminal negativity of the base as shown in typical electrocardiograms obtained with the string galvanometer: "Zum Schlusse wird dann die Basis wieder negativ aber das liegt nicht daran, dass dieser Teil dauernd negativ geblieben ist, wie man früher angenommen hat, sondern es ist der Ausdruck dafür, dass die Erregung wieder zur Herzbasis aufgestiegen ist." This view does not appear to commend itself to Kahn, who regards the evidence as "of the weakest." But the additional fact now brought forward indicates the point in the base to which the activity returns: this is, according to the foregoing experimental

results, the aortic base, which is the seat of a local but very marked activity, the last feature of the ventricular contraction.

THE WHOLE HEART.

The records, here described, being displacements of the meniscus of the capillary electrometer, do not in themselves show the actual amounts of potential difference; for this they need appropriate analysis, but such analysis is, in the present instance, difficult to achieve, owing to the steepness of the rise and fall in the first and second events. Until records have been taken on fast travelling plates the meaning of the records cannot, therefore, be fully ascertained. This consideration, however, does not invalidate the deductions which have been made from the inspection of the records as they stand, since experience has shown the extent to which such records may be safely utilised. They can undoubtedly be used for deducing such a thing as the change of sign of potential, and it is this change of sign which forms the more essential part of the present communication.

Until such analytic E. M. F. curves are made it seems inadvisable to compare in any great detail the present results with those which occur in the increasing number of communications on the subject of electrocardiograms. It is, perhaps, unnecessary to point out that such records obtained from the base and apex contacts, as those shown in Figs. 7 and 8, coincide in character with others obtained by the use of the electrometer, notably those of Samojloff, whilst, as regards the numerous electrocardiograms obtained with the string galvanometer, there is a general similarity between the two classes of records. In electrocardiograms with the whole heart interposed, arm and leg contacts for instance, the whole series of events, both auricular and ventricular, are present, whilst the present research deals only with the succession of events in the ventricle during its activity. I have, however, several records obtained from the rabbit's heart, which include the whole series, and it seems worth while to give one example of such a complete series although I have as yet made no special investigation of the succession of auricular events.

In order to connect the whole heart of the rabbit at two definite points, one contact was by means of the flexible tube thrust down so as to lie on the entry of the inferior vena cava into the right auricle. The other contact was then placed upon the right ventricle apex under which a piece of thin sheet india rubber was drawn.

The tissues largely short circuited the electrical effects, and the records are, therefore, small in size; but they show the general sequence of events as far as this can be judged by the movements of the electrometer.

An example is given in Fig. 20.

This record comprises the whole of the changes during a series of heart beats occurring at a frequency of 250 per minute. Each member of the

series constituting a beat comprises a double set of events marked as A and V.

Auricular.—The first set consists of those events which are shown in the record over each letter A: they are to be read from left to right, and are associated with auricular activity; each set consists of (1) a rapid upward movement; (2) a rapid downward movement; (3) a second upward rise; and (4) a final downward movement. It should be remarked that this does not correspond with the records obtained from the human heart by Einthoven and most subsequent observers, and which are referred by them to auricular events. On the other hand Kahn in a recent paper emphasises the variable form of the succession of the auricular events⁶.

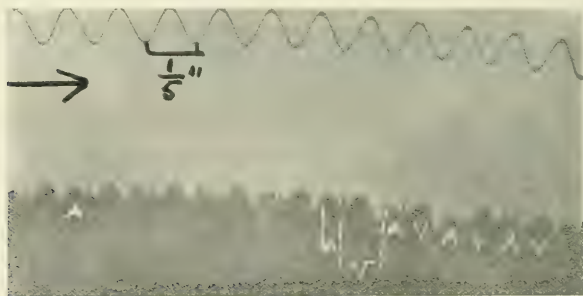


Fig. 20. Electrometer record of changes in a rabbit's heart with one contact on the right auricle near the inferior cava, the other on the right ventricle apex. Record of nine beats, all showing two sets of changes, a small auricular set above the letter A, and a larger ventricular set above the letter V. The rate of beat is 250 per minute. Upward movement signifies relative negativity at or near the auricle contact.

Ventricular.—The sequence of ventricle events during the part marked V comprises (1) a sharp upward movement; (2) a sharp downward movement; (3) a prominent second upward rise; (4) a downward movement marked in some beats but not in others. Thus all the events occurring during the ventricular contraction correspond with those given in Figs. 7 and 8, as displayed in the ventricle when one contact lies right athwart the base and the other lies on the apex. The ventricular effect is of the quadriphasic type (b, a, b, a). The remarkable circumstance is the character of the events which occur during what was undoubtedly the auricular contraction, viz., those described under (A). These resemble on a greatly reduced scale the general characters of the ventricular effects and are quite unlike the auricular events which appear in the electrometer records of the whole heart of the tortoise (see Fig. 1). It is difficult to give any satisfactory explanation

of these somewhat anomalous events during auricular contraction, of which I have many instances: the matter seems to me to demand a careful re-investigation with contacts at known points on the auricle.

At present the precise direction of the propagation of the activity in the mammalian auricle is, in spite of numerous electrocardiograms, still rather problematical. If, however, one is justified from the definite character of the ventricular records in concluding that the second delayed rise signifies a second delayed activity in the neighbourhood of the part first thrown into action, but due to a return of the wave of contraction to the aorta, then it may well be asked how can this explanation be applied to the auricular curve here given? In the ventricle there is an obvious part of the ventricle attached to each of the issuing great vessels which has, in the course of development, assumed a basal position, but what structural feature exists in the case of the auricle? It has occurred to me that the auricular appendages may possibly furnish the seat of a delayed activity, since it is clear that if the contraction starts from the vein entry it will spread not only towards the auriculo-ventricular groove but also over the wall of such appendages. I venture, therefore, to advance as a provisional explanation of the particular succession of events indicated in Fig. 20, this possibility, leaving it to future experiments to determine whether this supposition is correct.

One other source of difficulty is the circumstance already alluded to in connection with the tortoise heart (Fig. 1). It is easy to see in the slow beating heart of the tortoise the duration of the visible contraction auricular and ventricular. There is no doubt about the time relations of the two contractions, and the electrical events therefore demand the supposition that during quiescence one cavity wall acts as an indifferent conductor to the electrical changes in the other. How far this is the case in the quick beating rabbit's heart remains doubtful.

In conclusion, it is evident that as regards the second rise during the ventricular contraction, which forms such a conspicuous feature of all human electrocardiograms, its causation is probably related to the return of the contraction wave along the ventricle wall to the parts from which the aorta and pulmonary artery spring, and possibly to the walls of these vessels. If so, then as this part of the cardiac activity is of great importance from the point of view of the circulation, the degree to which it is appreciable in human electrocardiograms is a significant indication both of the efficient working of the heart and of the intracardiac pressure.

A further point is that the forms of electrometer curves shown in this communication are very various: but all the different varieties are explicable on the assumption that there are three successive active processes which overlap to different degrees, the amount of each overlap depending upon (a) the extent to which the contact embraces the chief seat of the active process; (b) the condition of the tissue.

SUMMARY.

1. Records have been obtained from the exposed surface of the tortoise heart beating *in situ*, by means of the capillary electrometer, which show that the propagation rate in the auricle is at 12° C., about 120 mm. in 1 sec., and in the ventricle about 90 mm. in 1 sec..

2. Records have been obtained from known points of the exposed surface of the rabbit's heart beating *in situ*, which show that the propagation rate on the ventricle varies from 3 metres per second when the heart is beating very vigorously, to 1 metre per second when beating slowly; as the heart fails the rate is still further reduced.

3. Records obtained from different parts of the surface of the tortoise ventricle show that the activity is not simultaneously developed during the natural beat, but is first developed at the groove, then at parts lying towards the apex, and finally in the part of the ventricle from which the aorta springs. These three successive developments are the cause of the peculiar triphasic electrical effects displayed in the records.

4. Records have been obtained with the capillary electrometer from known points of the ventricular surface of the rabbit's heart; these have the same general character whichever ventricle is investigated, provided that the relative positions of the contacts are alike as regards each ventricle.

5. The records from the rabbit's ventricle are quadriphasic (the sign changing four times), when one contact is athwart the base near the groove, whilst the other is on the apex; they are diphasic if the contacts lie on the lateral border and apex respectively; they are triphasic if the contacts lie one around the aorta and the other on the apex.

6. The interpretation of the triphasic records is shown to be in accordance with the view that each contraction begins in the general mass of base ventricular substance, that it then develops at the apex, and that it finally develops in the ventricular mass near the aorta (or pulmonary artery), with a possible extension into the wall of the aorta or pulmonary artery.

7. The interpretation of the quadriphasic record is that given in the preceding paragraph, but is associated with the diminished duration of the aortic effect as compared with the apex effect; this being more marked in proportion as the base contact recedes from the actual aorta or as the heart beat weakens in force.

8. If the base contact is actually around the aorta, the records become triphasic with a very marked terminal phase of a prolonged type; the full delayed base activity is thus very local.

9. The analogy between the present records and the well-known electrocardiograms obtained from man, etc., with the string galvanometer renders it extremely probable that the succession of electromotive events

indicated by these electrocardiograms is, like that found in the rabbit, similarly explicable by the presence of three successive activity developments. These overlap in time, and their sum is sufficient to account for the character of typical records.

BIBLIOGRAPHY.

- ¹ BAYLISS and STARLING. Internat. Monatsschr. f. Anat. u. Physiol., 1892, IX, 256.
- ² BURDON SANDERSON and PAGE. Journ. of Physiol., 1883, IV, 327.
- ³ GOTCH. Proc. Roy. Soc., 1907, B., LXXIX, 323.
- ⁴ GOTCH. Centralbl. f. Physiol., XXI, No. 15, 482.
- ⁵ GOTCH. Journ. of Physiol., 1904, XXXI, 1.
- ⁶ KAHN. Archiv f. d. ges. Physiol., 1909, CXXVI, 197, CXXIX, 291.
- ⁷ NICOLAI. Handbuch der Physiol. (Nagel), Bd. I., 1909, 824-826.
- ⁸ SAMOJLOFF. Archiv f. Anat. u. Physiol., 1906, Phys. Abth., Suppl., 207.

PAROXYSMAL TACHYCARDIA, THE RESULT OF ECTOPIC IMPULSE FORMATION.

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(*University College, London.*)

IN previous communications to this *Journal*, two cases of the auricular form of paroxysmal tachycardia and, in addition, certain experimental observations relating to paroxysms of rapid heart action in general have been recorded. In the following pages an account of a further example of clinical auricular paroxysms will be found with full details of the case in which the phenomenon has been observed.

The patient, who forms the basis of the remarks, originally attended the out-patient clinic of Dr. James Mackenzie. It is with pleasure that I acknowledge his generosity in placing not only the case but his own observations at my disposal.

HISTORY, ETC.

H. M. B., aged 41, a carpenter by trade and a married man, first attended the out-patient department at Welbeck Street in June, 1909, complaining of a general failure of health and attacks of giddiness and faintness. Ever since he has been under close observation.

The family history presents no point of interest. The father died at the age of 49, and the mother at 63, of ailments not definitely known. The patient has seven brothers alive and, so far as he knows, in good health. One brother was shot in South Africa. There were no sisters. Of seven children, six are alive and healthy; one died in infancy.

His previous health has been good, with the exception of an illness six years ago. He states that at that time he was laid up for six weeks, with influenza and right-sided pleurisy. In habit he has been neither temperate nor the reverse. Tobacco has been used sparingly. His work has been heavy and his hours long.

Present illness. For a month previous to his admission as an out-patient he suffered from failing health. Especially, he experienced attacks of giddiness and faintness, accompanied by a frequent sense of exhaustion. He was likewise distressed by frequent cold sweats with goose skin sensation, and a curious beating, which fluctuated, at the top of the chest. A slight dry cough, shortness of breath in walking even on level ground, and sleeplessness at night complete the list of the more prominent symptoms. He has had a certain amount of feverishness at nights.

Condition. 13-7-09. The patient is a frail poorly nourished man, with sallow complexion and clammy skin. The arteries present a slight grade of arteriosclerosis. The apex beat is ill-defined, and there is no pulsation in the epigastrium. On this account records from the chest

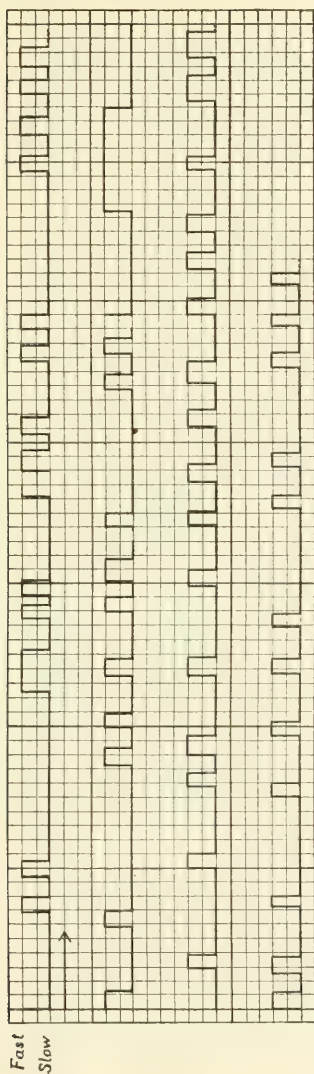


Fig. 1. The chart shows, in diagrammatic fashion, the relative duration of tachycardial and slow pulse rate. It has been constructed from a single curve, and covers 1 hour and 49 minutes. During this time 54 paroxysms occurred. The distance between adjacent ordinates is equivalent to 5 sec. The diagram reads continuously from left to right and from above downwards in 4 lines, and the record is unbroken, except where short stops or obscure tracing are indicated by broken lines.

wall are not obtainable. The percussion limits of the heart are as follows. The left border of dulness is $4\frac{1}{2}$ and the right 1 inch from the middle line. These limits show no definite variation with the onset or offset of the brief paroxysms of tachycardia which form the chief feature of the case. The heart sounds are clear, and there are no murmurs. The movements of the chest with respiration are fair; there is, perhaps, slight deficiency at the right apex. Over this apex also the percussion note is a little but definitely impaired, and both in front and behind numerous superficial fixed crackles are audible. The breath sounds are unaltered. There are no signs of old standing basal pleurisy. The liver shows no enlargement even while the heart is beating rapidly.

THE RADIAL CURVES.

The case is remarkable for the persistent recurrence of short attacks of tachycardia. An idea of the heart's action is best conveyed by means of a diagram (Fig. 1). The chart covers a space of 1 hour 49 minutes. The four lines of which it consists read continuously. It has been constructed to scale by measurements taken from a single and continuous curve. The ordinates are separated by 5 sec. intervals. The short vertical lines represent the onset or offset of a paroxysm; the abscissæ joining the summits of such lines indicate rapid heart action, while those joining their bases correspond to the slow periods. The diagram gives a clear impression of the relative duration of fast and slow rates, the actual lengths of the paroxysmal and slow periods, and the variations in each respectively. The chart, as a whole, may be regarded as a fair sample of the picture usually presented by the patient, though it occasionally happens that the paroxysms are less frequent or of longer duration. Thus, on occasion only two or three paroxysms have been noted during an hour of observation. The longest paroxysm recorded lasted about seven minutes, but paroxysms exceeding a minute in duration are rare. The shortest recorded attack consisted of four rapid beats in the radial curve. The rate of the tachycardia has varied between 133 and 184. It usually lies between 160 and 180. During the times when the pulse is slow it is rarely regular for many beats together, but is interrupted by extrasystoles which are accompanied by a pause not fully compensatory. Therefore, on most occasions it is impossible to calculate the fundamental sinus rhythm with any degree of certainty. Sometimes the pulse is perfectly regular over lengths of curve of a half minute or more, and then the rate lies between 76 and 88.

A short strip of the radial tracing is given in Fig. 2. It shows three paroxysms breaking into the usual slow and irregular rhythm of the slow periods. The patient is usually conscious of both onset and offset of the tachycardia, when his attention is closely directed to it. While lying supine he was requested to raise his arm at the onset and to lower it at the offset of each attack. The raising and lowering of the arm were marked by hand on the curve as it was taken, and these rough signals are shown on the accompanying curve. Recognition of the alteration of heart rate was attained by the patient by his perception of the associated beating in his chest.

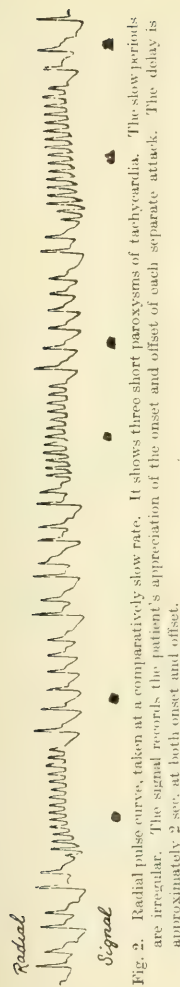


Fig. 2. Radial pulse curve, taken at a comparatively slow rate. It shows three short paroxysms of tachycardia. The slow periods are irregular. The signal records the patient's appreciation of the onset and offset of each separate attack. The delay is approximately 2 sec. at both onset and offset.

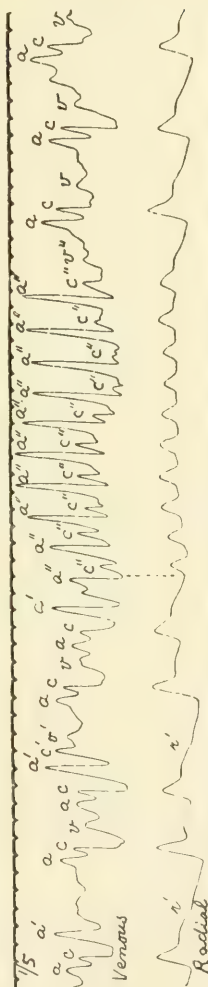


Fig. 3. Faster curve taken on the same day. Venous and radial curves are shown. The slow period at the commencement is interrupted by auricular extrasystoles (a'). The paroxysm is started in the auricle, as evidenced by the waves a'' . There is a slight rise of B. P. subsequent to the onset of the attack.

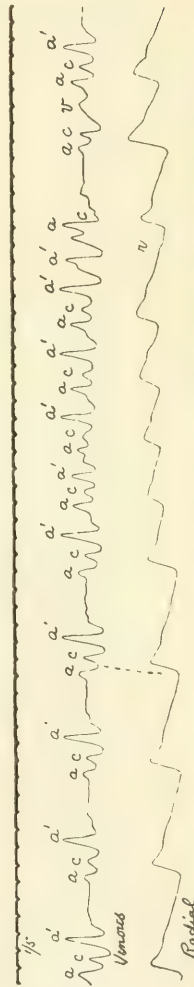


Fig. 4. Four auricular extrasystoles, probably awakening no ventricular response, but interfering with the sinus rhythm, are shown to the left. They are succeeded by interpolated auricular extrasystoles, in which neither sinus nor ventricle are affected.

The attacks are most frequent when the patient has been at work, and after exertion of any kind. They tend to subside, but never disappear entirely, after he has been recumbent for several hours or longer. On one occasion, while under the observation of Dr. Mackenzie, and while the paroxysms were relatively infrequent, it was noticed that they were brought on by swallowing. Numerous observations were made at the time, and although the effect of a swallow was not invariable, yet the movement was so frequently succeeded by a paroxysm that no doubt remained but that the latter directly resulted from it.

Treatment, apart from improving his general health, has been without avail.

POLYGRAPH RECORDS.

The action of the heart between the paroxysms is, as has been previously stated, very irregular. The irregularity is due to the interruption of the normal sinus rhythm by beats, which simultaneous radial and venous curves show to be of the nature of auricular extrasystoles. The frequency of these interruptions of the sinus rhythm is very variable: there may be only occasional extrasystolic contractions: they may alternate with one or more of the normal beats, or may occur frequently and in haphazard fashion. *They are invariably auricular in origin*, and are almost always very numerous. Further, they are isolated and (leaving the paroxysms out of consideration) do not occur successively or in groups. Studied in the radial curve they are found to affect the pressure in the artery to a small extent or not at all (some indication of them is to be seen in the radial curves of Figs. 3, 5, 6 and 8, where they are marked r , while in Fig. 4, as also in several of the above mentioned figures, they leave no trace of their presence). In the venous curve the extra wave a' is always well marked, and it is often followed by waves c' and r' , which are attributable to the ventricular response. At times the wave a' appears to stand alone, and in these instances (cp. Fig. 4) the impression is conveyed that we have to do with a failure of conduction to the ventricle. That the waves a' , in Fig. 4, for example, are in reality due to auricular contraction, and that they are not anomalous r waves, is easily demonstrated. They are identical with the a' waves of the auricular extrasystoles, and occur earlier after the preceding c wave than do the true v waves*. The comparison may be made in Fig. 4, or in Fig. 6. They are taller than v waves, and also reach to a greater height than the a waves of the sinus beats. This is obviously attributable to the fact that they occur before ventricular systole is complete. Lastly, the lengths of the cycles with which they interfere are compatible with those of cycles interrupted by extrasystoles reaching the ventricle; and they are unaccompanied

* Attention is specially directed in this connection to the relation of the fall of the wave, a or v as the case may be, to the preceding c wave.

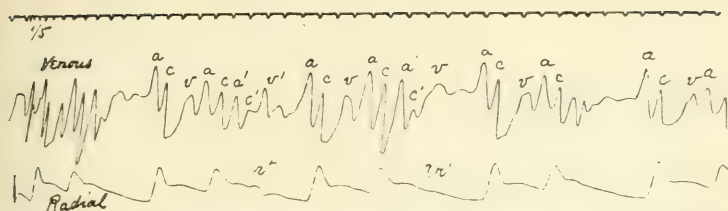


Fig. 5. Venous and radial curves during a slow period. Auricular extrasystoles are shown. The stops may be used in checking measurements in this and other figures.

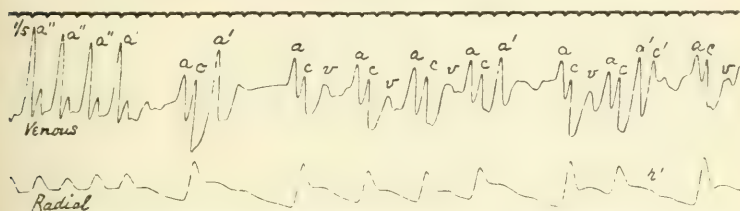


Fig. 6. The end of a paroxysm, showing the termination in a long pause, which is succeeded by a gradually accelerating sinus rhythm, itself interrupted by auricular extrasystoles.

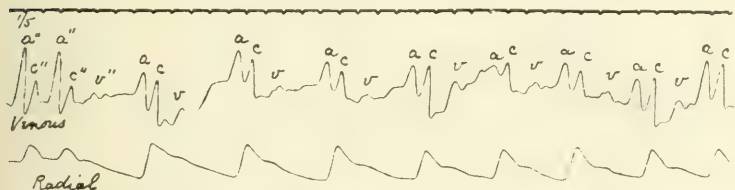


Fig. 7. The same as Fig. 6, except that during the slow period no extrasystoles occur.

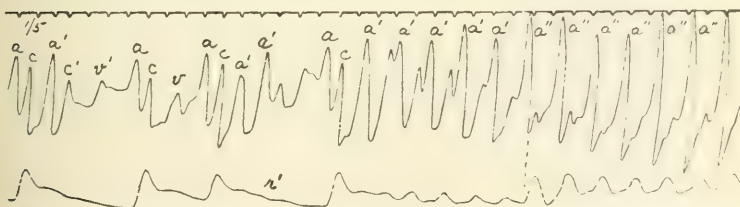


Fig. 8. The onset of a paroxysm. The slow period to the left is irregular as a result of auricular extrasystoles. Tachycardia starts in the auricle, towards the centre of the figure; it consists of a series of extrasystoles (a') each awakening an abortive ventricular response. The curve changes abruptly to the true paroxysm (a'').

by a first heart sound. The suggestion, offered by these facts, that we are dealing with blocked auricular extrasystoles in some of the examples shown (the failure of conduction of such beats has been already described by Hewlett²) is conclusively proved by the electrocardiograms which are to be discussed later.

The heart's action during the paroxysms is equally clear. It is illustrated in Figs. 2, 3, 8, and 9. The heart's mechanism is always the same. The paroxysms are shown to start in the auricle, for each beat of the ventricle is preceded by a contraction of the former. The *a-c* interval during the paroxysms is about $\frac{1}{3}$ sec.* that is to say, it is of about the same length as during the slow periods. The excessive height of the *a* waves is assigned to the shortened Vs-As interval, or, described in terms of the venous pulse, to *a* falling back on *v*. The auricle contracts before the preceding ventricular systole is complete. During the paroxysms alternation of the ventricle is occasionally present. As examples of this phenomenon have already been published in the first number of this *Journal*, further illustration of the point is not considered necessary. The lesser beats, as in previously reported cases, may vanish almost entirely.

A notable feature of the paroxysms, shown in Figs. 2, 3, and 8, is the general rise in the curve as the paroxysm proceeds. It is an indication of a slight increase of blood pressure consequent upon the more rapid heart action.

The transitional portions of the curves are of special interest. The paroxysms commence in a variety of ways. The auricular extrasystoles are always frequent directly before the onset. Fig. 3 shows a comparatively simple form of onset. The slow rhythm is disturbed by *effective* auricular extrasystoles (or extrasystoles which cause ventricular responses). Two of such beats are shown in the figure. Following these beats are two normal responses, then an auricular extrasystole, and from this point onwards regular auricular waves appear (*a''*) each of which awakens a ventricular response. In some instances two or more extrasystoles may directly precede the paroxysm, and in such cases a long pause in the radial curve, with or without abortive waves upon it, is found as a precursor of the paroxysm. In Fig. 8 a tracing is given in which a slow period is at first interrupted by extrasystoles which are effective; during the second radial pause two beats of the same nature are interpolated and the pause ends in a normal response. Following upon this is a succession of five extrasystoles, and these in turn are succeeded by the true paroxysm (of which seven beats are shown). The expression true paroxysm is employed because the first five beats lie lower in the curve, they do not raise arterial pressure, which tends to fall away, as do the remainder of the beats, and the change from one type

* There is a slight variation in the intervals in many of the curves, more especially the electrocardiographic, which tends to show that the normal As-Vs distance is greater with the abnormal than with the sinus beats (cp. Fig. 17), but it is not always well marked.

to the other is marked by an abrupt rise in the curve. Further reasons for this differentiation will be stated later. The same phenomenon is visible in the opening beats of the paroxysm shown in Fig. 9.

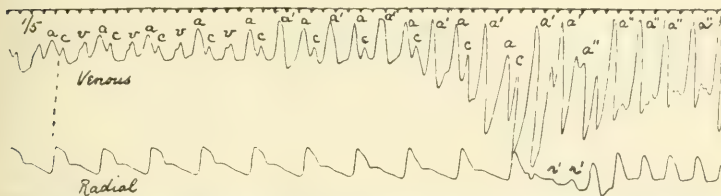


Fig. 9. Onset of a paroxysm. The rhythm and sequence is at first normal. Interpolated auricular extrasystoles appear suddenly in the curve. None of these reach the ventricle. Between the interpolation stage and the paroxysm proper (of which 5 beats are shown) two abortive radial curves are seen. They are the result of successive auricular extrasystoles.

We may now turn our attention to Fig. 4. The first beats of this curve are blocked auricular extrasystoles*. These extrasystoles, like those which awaken ventricular responses, interfere with the sinus rhythm and produce the diastolic pause indicated in the radial pulse. At times the disturbance of the sinus rhythm is absent and on such occasions *interpolated auricular extrasystoles* occur. Fig. 4 illustrates the condition very clearly, and shows the sudden passage of one mechanism to the other. Moreover, they are interpolations of a very curious nature. For they affect neither sinus nor ventricle. Every interpolated beat is blocked†. The disturbance is strictly limited to the auricle, and the regular impulses transmitted across this chamber to the ventricle are in no way interfered with‡. At the end of the interpolation period the radial pulse shows an increased pause. It is probable that at this time two auricular extrasystoles occur, and that the last beat of the pair alone yields a ventricular response, though the response is doubtful. Fig. 9 confirms the explanation adopted in the case of Fig. 4. The tracing commences with the normal sinus rhythm; each ventricular contraction is associated with *a*, *c*, and *v* waves. Later, in the curve auricular extrasystoles suddenly appear, and they affect neither sinus nor ventricular rhythms. Apart from the mode of its onset, the curve, up to this point, is in every way similar to Fig. 4. Towards the end of the curve also the extra beats are seen in succession, and they give rise to two small radial waves, *r'* and *r''*.

* The evidence for the blocking of these particular beats is, perhaps, inconclusive: the statement is based on the fact that blocked extrasystoles are known to occur frequently in this case (from an examination of the electrocardiographic curves), and upon the absence of *c'* and *r'* waves in the curve.

† This is clearly the case, for otherwise the *a* and *a'* waves would be equally prominent.

‡ More recently records have been obtained from another patient, in which interpolated auricular extrasystoles were present, but in which each extra beat was transmitted to the ventricle.

The curve then passes into the paroxysm proper in which the auricular beats are evenly spaced and give rise to regular responses. From these curves, and from a large number of others in my possession, it is recognised that Fig. 4 represents the preliminary stage which often precedes the appearance of the ventricular paroxysm (as in Fig. 9). This statement is based on the following facts. First, that apart from similar examples (and they are comparatively rare) interpolations are never met with except as direct precursors of a paroxysm. Secondly, that it is common for the paroxysms to start in this manner. Thirdly, that the paroxysms are very variable in length, and may be cut short at any stage. Fourthly, that apart from this solitary instance successive extrasystoles have never been met with except directly prior to the onset of a paroxysm. We have to acknowledge in the first place that the paroxysms are foreshadowed by the occurrence of an auricular tachycardia, consisting of alternate responses to sinus and alternate interpolations, and that this premonitory tachycardia is of a very similar rate to that of the paroxysm itself (though it is rarely identical with it). At the same time we have evidence that the paroxysms and the interpolation periods are essentially different, though closely bound up together. This evidence as at present advanced is as follows. Periods of interpolation are always separated from paroxysm by an interval, in which one, two or more of the insignificant r' waves appear in the radial pulse. Secondly, beats of the paroxysm itself are never blocked.

The termination of the paroxysms is of equal interest. It is illustrated in Figs. 3, 6, and 7. The paroxysms invariably end in a prolonged pause. The length of this pause is variable within certain limits, and is occasionally interrupted by the occurrence of a smaller beat of the type seen at the commencement of the paroxysms. As a rule such interruptions are absent. Careful measurements were made in several strips of curve in which paroxysms were frequent, for the purpose of ascertaining the relation between the pause following the paroxysm and the pause following extrasystolic contractions during the slow periods. On account of the variation in presphygmie interval known to accompany extrasystoles, the measurements were made in the venous curves from a' or a'' waves to a waves. The results are embodied in the table. In the first column the length of the pause following an auricular extrasystole is given. The extrasystole was chosen from the centre of a slow period, and may, therefore, be said to succeed one paroxysm and precede the next. In the fourth column the pause following the succeeding paroxysm is given. It will be seen that the pauses vary slightly and in approximately the same degree, and that the figures given in the two columns are in close agreement*.

The average for the paroxysmal pauses exceeds that for the extrasystolic by $\frac{0.07}{5}$ sec., a practically negligible quantity. In a previously reported case of paroxysmal tachycardia, considerable stress was laid upon the occurrence

* The variation in individual cases is scarcely greater than the error in measurement.

TABLE OF PAUSES.

| Length of pause in ½ sec., following AEs. between the paroxysms. | Rate of paroxysm per minute. | Length of paroxysm in sec., | Length in ½ sec. of pause at end of paroxysm. |
|---|------------------------------------|-----------------------------------|---|
| — | 169 | 16.2 | 4.5 |
| 4.4 | 161 | 23.5 | 4.5 |
| 4.5 | 166 | 16.6 | 4.3 |
| 4.6 | 157 | 3.2 | 4.3 |
| 5.2 | 165 | 5.2 | 4.5 |
| 4.0 | 182 | 19.4 | 4.4 |
| 4.4 | 180 | 4.6 | 4.3 |
| 4.4 | 181 | 5.9 | 4.5 |
| 4.6 | 163 | 6.5 | 4.4 |
| 4.7 | 169 | 6.9 | 4.6 |
| 4.5 | 170 | 8.7 | 5.0 |
| 4.4 | 167 | 8.0 | 4.0 |
| 4.1 | 165 | 4.8 | 4.1 |
| 4.4 | 167 | 4.2 | 4.6 |
| 4.2 | 168 | 6.1 | 4.9 |
| 4.1 | 169 | 5.5 | 4.3 |
| 4.1 | 170 | 5.4 | 4.1 |
| 4.5 | 170 | 6.1 | 5.1 |
| 4.3 | 165 | 4.8 | 4.5 |
| 4.4 | 166 | 6.4 | 4.4 |
| 4.4 | 167 | 6.0 | 4.6 |
| 4.5 | 167 | 4.3 | 4.7 |
| 4.4 | 165 | 4.2 | 4.6 |
| Average 4.41 | — | — | 4.48 |

of these pauses, but the wide variation then observed in them would not allow of their co-relation with any other measurement. The reason of the difference in the two patients is probably to be found in the fact that we are at present dealing with short paroxysms, while in the earlier case the tachycardia always persisted for a long while. The cause of the pause is now more obvious. It may be regarded as identical in extrasystole and paroxysm, and may be interpreted as the time taken for the last impulse to reach the sinus, plus the time taken for the formation of a fresh sinus impulse (Cushny and Matthews¹). The length of the post-paroxysmal pause would be readily accounted for in this way were it not that an additional phenomenon is present. Fig. 7 shows the termination of a paroxysm in uninterrupted normal rhythm. The end of the paroxysm is succeeded by a decreased pulse rate, followed by a return to the normal. A slow sinus rate as a sequence to the paroxysm is invariable, but it is fugitive. Similar retardation of the pulse at the termination of a paroxysm has been noticed as of constant occurrence in another patient; it was absent in the case previously reported, and also in the instance of the paroxysms produced experimentally.

The phenomenon reminds us of the preliminary slow rate of a newly awakened idioventricular rhythm, and of the gradual development of a faster and more constant rate. The explanation is insufficient in that it fails to account for the absence of prolongation of the post-paroxysmal pause. It might be attributed to a reflex increase of vagal tone, and the absence of retardation in the experimental instance would harmonise, for the vagi were divided. The facts do not warrant anything but the most tentative conclusion; emphasis is laid upon the slowing, because it stands in contrast to the acceleration which often follows the single extrasystole. Its presence at the commencement of the slow period fully explains the variation in the lengths of the beats of the *interrupted* rhythm which usually succeeds the paroxysms (an example of which is shown in Fig. 6). It served as an additional reason for the measurement of extrasystolic pauses lying in the centre of the slow periods only.

ELECTROCARDIOGRAPHIC CURVES.*

We may now conclude the description of the investigation of this case by referring to the electrocardiographic curves. So far, and in the main, we have been able to elucidate the following facts. We are dealing with a tachycardia of auricular origin, and the abnormal mechanism during both paroxysmal and slow periods is attributable to ectopic beats arising in auricular tissue. We have also very suggestive evidence that we have to do with ectopic beats of several kinds. This suspicion at once becomes a conclusion with the galvanometer curves before us. There are at least three varieties of ectopic beats.

The interpretation of the accompanying curves, depends largely upon the view adopted as to the nature of the electric curve yielded by an auricular contraction starting in an abnormal position in the auricle. In my first paper upon paroxysmal tachycardia the possibility that an abnormal auricular curve would result was fully recognised, and in the second paper the proof of the proposition was furnished by the example of a retrograde contraction. Fig. 10 shows simultaneous venous and electrocardiographic curves, and allows of a very exact analysis. The first two beats, which are shown, are of normal sinus origin. But there is a notable difference between the T waves of the two ventricular systoles. The second lifts more abruptly, is shorter, and is followed by a prolonged pause. The venous curve shows that an auricular extrasystole has occurred, and it has been ineffective. The interpretation is completely borne out by Fig. 12, where the auricular extrasystole though effective produces precisely the same deformation of the wave T. To proceed with Fig. 10, the next two beats are normal, the following

* The electrocardiographic curves were taken at University College Medical School, and the expenses involved in their production have been defrayed by a grant from the British Medical Association.

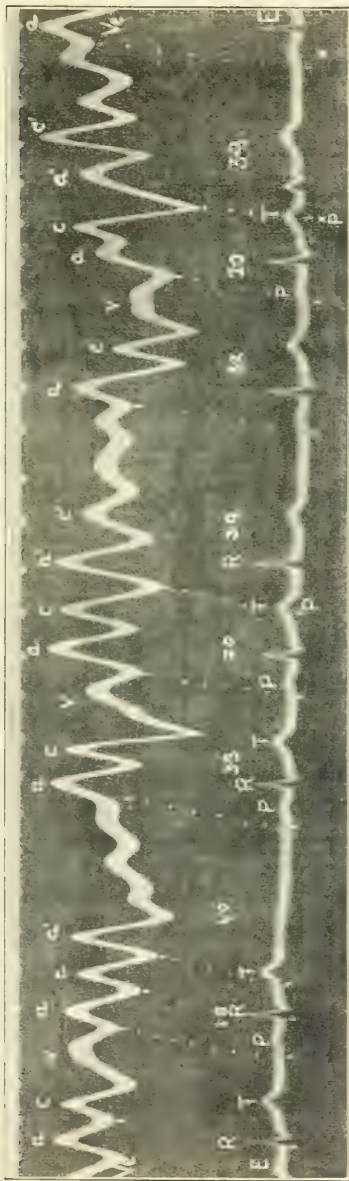


Fig. 10. Simultaneous venous (Vc) and electrocardiographic (E) curves. As in all figures the time (top curve) is in $\frac{1}{5}$ sec.

From left to right, two normal beats, a blocked auricular extrasystole, a long pause, two normal beats, an auricular extrasystole (Type I), a pause, two normal beats, an auricular extrasystole (Type II), a pause and a commencing normal beat, are shown. Each auricular extrasystole deforms the preceding T wave. The space figures are in terms of fifths of seconds.

one is premature. It is an auricular extrasystole (Type I), and it likewise deforms the preceding T wave*. But the alteration of this T wave by the auricular contraction is different from that of the T wave of the second beat,

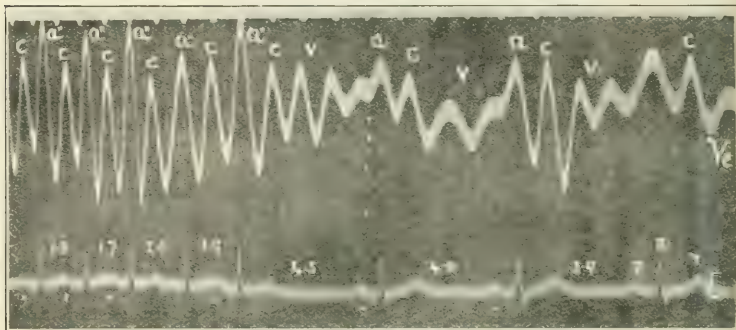


Fig. 11. The end of a paroxysm. Acceleration is well shown in the slow period. As in Fig. 10, and in succeeding figures, small white crosses are placed beneath downward notches in the curve, which represent auricular contraction.

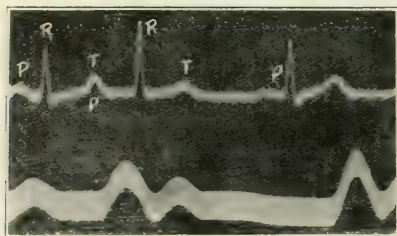


Fig. 12. Electrocardiogram and radial curve. A normal beat, in which the auricular notch is well-marked, is succeeded by an auricular extrasystole of Type I. It causes the deformity of the first T wave. The extrasystolic R is large. Prolongation of the As Vs interval is distinct in the case of the extrasystole.

and this is due, as is the efficiency of the auricular contraction in creating a ventricular response, to the later occurrence of the extra beat. The next two beats of the curve are normal. They are succeeded by the third auricular

* The peak R of the extrasystole is taller than that of the normal beats, yet the pulse beat accompanying such beats is often absent (Fig. 12). The same disproportion has been met with clinically in heart alternation, the large peak R may correspond to the small pulse beat.

extrasystole (Type II) to be found in the curve. It is known to be auricular by an examination of the accompanying venous curve, and from the fact that it deforms the T wave which lies to the left of it*. We have proof, therefore, of auricular extrasystoles of two types, and may now turn

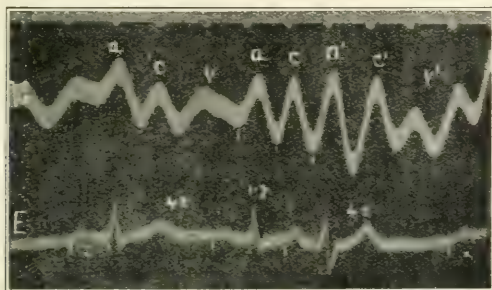


Fig. 13. Venous and electrocardiographic curves. Two normal beats are succeeded by an auricular extrasystole of Type III.

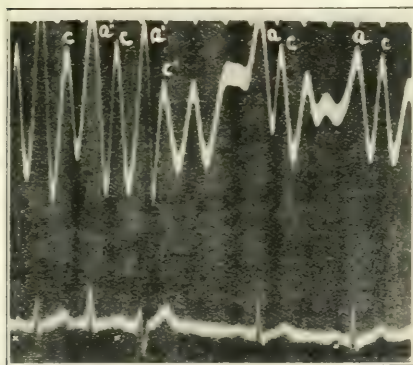


Fig. 14. The end of a paroxysm. The paroxysm terminates in an auricular extrasystole of Type III.

* The dotted line drawn to T is not quite correctly placed. Its upper end should terminate more to the right. The upstroke, to the bottom of which it is drawn, is in reality the upstroke of v. The correction may be checked from the peaks of the venous waves.

to Fig. 13. In this curve an example of the third type (Type III) is shown. Precisely similar arguments to those already employed demonstrate it as an auricular extrasystole. The same form of beat occurs in Fig. 14, where it terminates the paroxysm*. Attention is now drawn to a character of the curves, which, though unexplained, is of peculiar service. We have seen that the deformation of the wave T by extrasystolic auricular beats consists of a slight notching in the positive or downward direction. This notching is far more distinct in some curves than in others, and is clearer in the originals than in the reproductions. Moreover, it is plainly seen in many of the *normal P* curves (cp. Figs. 10, 11, 14, 15, 16, and 17). It serves to identify the auricular contraction, but while it occurs in the centre of the normal auricular curve P, it appears to be the sole representative of the abnormal auricular contractions, and is situate at the starting point of these beats†. In the accompanying curves the notch has been marked, where clearly visible in the originals, by a small white cross.

The paroxysms themselves, portions of which are shown in Fig. 11 (first part), Fig. 14 (first part), and Fig. 16 (last part), consist of beats bearing a close resemblance to the extrasystole of Type I (and shown in Figs. 10 and 12). The paroxysmal type is shown most clearly in the last four beats of Fig. 16. The apparent difference between beats of this nature and the extrasystolic type shown in Fig. 12, consists in the deformation of the associated T waves by the deep notching resulting from the auricular contractions. The same general features are visible in Figs. 11 and 14. Now the type of extrasystole referred to (Type I) is the rarest of all during the slow periods. The commonest type is that shown at the end of Fig. 13 (Type II), and the third type with the deep S depression is almost as common. As it may be said that the paroxysm is constituted by beats‡ similar to or identical with the rare type of extrasystolic beat, emphasis may be laid on a caution formerly expressed. This was to the effect that the conclusion, that beats of a paroxysm and those interrupting the slow periods are identical, is not warranted in the absence of galvanometric evidence.

In concluding a description of the facts presented by this case, several other points must be noted. Fig. 15 is an example of an alternation of

* Termination in this manner is quite exceptional.

† Explanations parallel to those which have been offered for the split P wave in mitral stenosis naturally suggest themselves, but they would lead at present to deductions too vague to be of value.

The absence of any indication of auricular contraction other than the dip (which is obviously a special feature in this particular case) throws a new light upon the case reported in this *Journal*, p. 51. It is no longer possible to attribute the wave marked P in Fig. 5a to auricular contraction alone. There is every possibility that it may represent a T or deformed T wave. This reservation affects the remarks made in the first paragraph of p. 70.

‡ The paroxysmal beats are always of this type. It is remarkable that in three cases of auricular paroxysmal tachycardia, the ventricular portions of the paroxysmal electrocardiographic curves have always been of the normal type (Type I) and never of the abnormal types (Types II and III). They differ from the normal beats in the corresponding patients by the increased prominence of R, and this despite the faster heart rate prevailing.



Fig. 15. Electrocardiographic curve showing alternate normal and extrasystolic contractions. The latter are all of auricular origin. The auricular notches are very clear. The "bigeminy" abruptly alters. It contains beats of Type III at the beginning, and of Type II at the end.

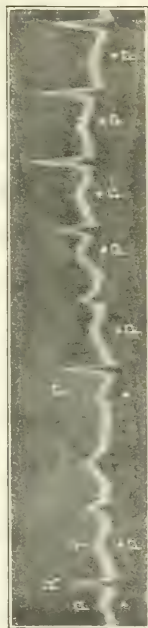


Fig. 16. From a curve continuous with Fig. 15. The onset of a paroxysm (last 4 beats) is shown. The second auricular extrasystole (of Type II) is shown directly preceding the paroxysm.

normal beats and auricular extrasystolic contractions; the remarkable feature of this curve is the sudden change in the type of the ectopic beats. While a continuous "bigeminy" is present, it is of one type to the left, and of another and distinct type to the right*. The curve directly preceded a paroxysm, of which the commencement is seen in Fig. 16. The time tracing unfortunately failed in these curves, but the spacing of the beats can be gauged from the rate of the paroxysm shown at the end of Fig. 16. The second extrasystole of Fig. 16 commands especial attention. The beats adjacent to it are separated by an interval approximately equal to that between alternate beats of the paroxysm itself. It might be regarded as an interpolation, but it differs from those shown in Figs. 4 and 9 in two respects. In the first place it is effective, and in the second place the P' wave belonging to it is separated from the preceding P wave by a shorter interval than from the succeeding P wave. The beat belongs to those discussed as precursors of the paroxysm of Fig. 9. The presence of this beat at the commencement of the paroxysm helps to justify the previous conclusion that those insignificant beats at the commencement of tachycardia which contrast so markedly in the radial curve with the beats of the paroxysm proper are of a different nature to the paroxysmal beats†. The differentiation is of importance, for, if it is accepted‡, we may conclude that only those beats which appear in the fully developed form in the radial curve are paroxysmal. When a paroxysm of four rapid beats appears in the radial curve, even if it is preceded by tachycardia in the auricle, we have to assume that they are the offspring of four auricular ectopic beats, and that these four alone belong to the ectopic rhythm proper.

The interpretation of the curves involves two assumptions; first, that the auricular tachycardia displayed by Fig. 4 is not an ectopic rhythm, but consists of interpolations. This is evident from the curves which precede such periods, and from the strict separation of such periods from the paroxysms proper.

The second assumption is that the paroxysm itself does not consist of interpolations. It is perfectly obvious that it is not composed of

* Several different combinations of this change in the type of the bigeminy have been noted in this patient.

† Considerable stress is laid on the radial differentiation; experience shows it to be of great value. The appearance of successive extrasystoles directly before the onset of a paroxysm, and at this point only, has recently been observed in another patient, and the electrocardiographic evidence is in this instance conclusive. A suggestion is offered that the preliminary successive extrasystole may constitute the exciting cause of the paroxysm itself.

‡ Later observations upon the case here reported have conclusively shown the nature of the beats referred to. Several electrocardiographic curves demonstrating the onset of a paroxysm in successive beats of Type II have been obtained.

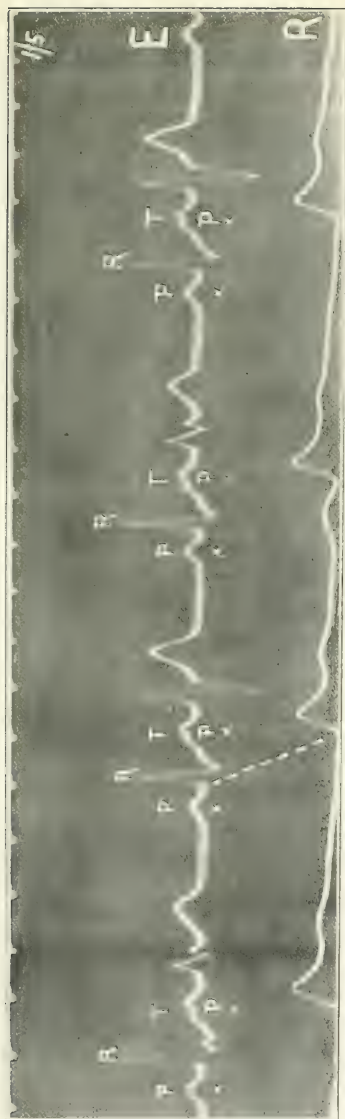


Fig. 17. Linear. "bigeminy," consisting of normal beats and auricular extrasystoles, is shown. The abnormal beats are of Types II and III; they are arranged alternately between the normal beats.

interpolations of the two commoner types, but it is more difficult to exclude a series of interpolations of the type shown in Fig. 12. Nevertheless we are justified in excluding this possibility also. When this type of beat occurs singly it does not affect the arterial pressure to any appreciable extent (Fig. 12). Interpolations when found in other parts of the tracings are never effective in producing ventricular response. Further, the beats of the paroxysm are never blocked, although the paroxysmal rate is subject to considerable variation. Again, the beats of the paroxysm are quite regularly placed, and the radial curves do not exhibit alterations in excursion which would be expected if alternate beats were produced by distinct mechanisms. Finally, if this view of interpolation is adopted the beats of the paroxysm which have to be assumed as of normal sinus origin may be easily ascertained, and, as a result, it is found that the last beat of the paroxysm has at times to be assumed as a normal beat, and at times as an extrasystolic contraction. If such were actually the case the uniformity of the post-paroxysmal pause would not be expected.

Fig. 17 is an example of the alternation of two types of extrasystole in a bigeminal curve. Several combinations of the three types have been met with, and they produce similar pictures.

In this figure the notches, representative of auricular contraction, are particularly well marked. But they are more clearly shown in the case of the extrasystolic contractions. On the other hand, in Figs. 15 and 16 the depressions are equally conspicuous in both. Fig. 17 was taken at a later date.

GENERAL DISCUSSION.

The present instance of paroxysmal tachycardia is remarkable for one feature at least. It forms a useful connecting link between those instances in which paroxysms of an hour or a day are the rule, and cases in which short runs of ectopic beats are alone found. In a previous paper I have expressed the conviction that there is no essential difference in the nature of the individual beats of the forms of paroxysmal tachycardia considered, and the beats hitherto spoken of as extrasystolic contractions, and have brought forward experimental evidence in favour of this view.

In the present case we have an example of paroxysmal tachycardia in which the ectopic rhythm, upon which it depends, may last for four beats only or for several minutes. The fact that at one time but a few beats appear,

and that at another a long continued succession of beats is found, cannot, therefore, be held as an essential or distinguishing factor. The chain of instances is now complete from the single extrasystole to the groups of several successive extrasystoles, to instances of paroxysms of short duration, and eventually to those which are prolonged for days or even weeks.

The second feature of importance in the present case is the level at which the ectopic rhythm arises. We may certainly place the focus of origin in the auricular tissue, and in consideration of the abnormal character of the electric curve may conclude that the auricle has contracted in an abnormal direction. This is tantamount to a conclusion that the starting point of auricular systole lies at some distance from the normal centre of impulse formation, a conclusion which receives support from the length of the pause following the individual paroxysms. If we accept the upper regions of the auricle as the normal centre of impulse formation, we must, as a consequence, place the origin of the present paroxysms in the middle or lower level of the auricle. The last-mentioned region is improbable, but the reasons for this opinion cannot be entered upon at the present time: they are based upon the detailed examination of another instance of ectopic paroxysmal tachycardia which will be fully described at a later date. Suffice it to say that in the new instance the auricular curve in the electrocardiograms is completely inverted, and that there is strong presumptive evidence that the seat of origin is in the lowest level of the auricle. The view previously expressed that ectopic rhythms may arise at any level of the heart is thus confirmed.*

The appearance of three separate types of ventricular electrocardiogram, each as a result of an auricular extrasystole, remains to be discussed. It is a fact for which a complete explanation fails at the present time, and involves questions which can only be solved by appeal to experiment. It has been customary to assume (1) that all beats of the ventricle of supraventricular origin are conveyed to that chamber along a single path, and that they enter the ventricular musculature by the same doorway. It has also been supposed (2) that all systoles of the ventricle which arise at a fixed point in the musculature will, *ceteris paribus*, yield the same and a distinctive type of electrocardiogram. Therefore, it is further assumed that all beats of supraventricular origin will yield the same type of electrocardiogram. The evidence of this case is directly opposed to the last conclusion, and there seems to be no alternative but to seek for some flaw in the propositions upon

The conclusion, based in part on an undescribed case, is necessitated, for the case in question will be utilised subsequently in the discussion of an entirely different problem.

which this conclusion is based. Both the original propositions (1 and 2) are supported by considerable evidence, evidence which is well known and which it would be out of place to discuss at the present time. Kraus and Nicolai have stated that auricular extrasystoles started experimentally in right and left auricle are accompanied by ventricular electrocardiograms of different forms. Their observation, with which the present clinical facts are consistent, is equally at variance with our present views of the cardiac mechanism, or with our present interpretation of electrocardiographic curves.

The several types of beat described in this paper cannot be explained as the result of varying time relations. They cannot be identified except by electrocardiographic means. A suggestion which can be offered in explanation of them is that they may arise from separate foci in the auricular walls; the location of the exact sites of origin of the impulses is beyond the limits of this communication.* In regard to the questions which their presence raises the writer inclines to the opinion that the explanation must be sought in a revision of our present ideas of the possible mode (or modes) of conduction from auricle to ventricle.

SUMMARY AND CONCLUSIONS.

1. A case of paroxysmal tachycardia, due to ectopic impulse formation, is described, in which it is believed that the source of impulses lies at a point near the physiological centre of the main mass of auricular tissue. The case is exceptional in that the paroxysms are short and of extremely frequent occurrence. The case forms a connecting link between other instances in which either single ectopic beats or ectopic rhythms of long duration interfere with the normal mechanism of the heart. The case supports the views already adopted that there is no essential distinction between extrasystolic and paroxysmal beats, and that paroxysmal tachycardia which is due to ectopic impulse formation may arise at any level of the heart.

2. Auricular extrasystoles met with clinically give rise to ventricular contractions of at least three distinct forms, as evidenced by the electrocardiographic curves which they yield.

* The question of accurate location is the more important as very similar, if not identical, types have been observed, singly or together, in other cases. In other words, the present case is by no means phenomenal in this respect.

3. A clinical instance of blocked auricular extrasystoles (Hewlett) and of interpolated auricular extrasystoles is described.

BIBLIOGRAPHY.

- ¹ CUSHNY and MATTHEWS. Journ. of Physiol., 1897, xxi, 213-230.
- ² HEWLETT. Journ. Amer. Med. Assoc., 1907, XLVIII, vol. 48, 1597-8.

INDEPENDENT VENTRICULAR RHYTHM: HEART-BLOCK AND THE STOKES-ADAMS SYNDROME WITHOUT AFFECTION OF CONDUCTIVITY.

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THAT the ventricles are capable of starting and maintaining a rhythm of their own when deprived of the normal stimulus from the auricles is well known and quite sufficiently attested both by morbid conditions in human beings and by the results of experiments in animals. Theoretically, it is probable that a stimulus, which does not act because the more rapidly built up stimulus at the great veins never permits of it, is constantly generated in the ventricles. With the removal of the stimulus from above, the ventricular stimulus comes into play and starts a rhythm of about 36 per minute. It might, however, be argued that the ventricles only started building their own stimulus when the necessity for this stimulus production was forced on them by the withdrawal of the normal stimulus from the veins. This latter view is supported to some extent by the fact that in animal experiments a sudden withdrawal of the venous stimulus is followed by a stoppage of the ventricles and it is only after an appreciable interval that the ventricles start beating on their own account. The sudden establishment of complete block between auricles and ventricles has also been advanced as an explanation of the syncopal and epileptic attacks, occurring in cases of partial heart-block, in which the ventricles cease to beat for a more or less prolonged period. Therefore, it becomes important to collect definite evidence of the existence of stimulus production in the ventricles while they are still under the influence of the sinus rhythm. This is naturally a difficult matter as the normal ventricular rhythm is only about half the rate of the normal sinus rhythm, so that opportunities for the ventricular rhythm to show itself must be very rare. In animal hearts v. Tabora¹ found that digitalis caused a block between auricle and ventricle, and that sometimes in consequence of this block there was a sufficiently long interval after a ventricular beat to allow the ventricular stimulus to cause a beat before one could descend from the auricles. Increasing the irritability of the ventricles while the vagal tone is increased, as in Cushman's² experiments with aconitine, leads to the ventricles imposing their rhythm upon the auricles; a fact which is strongly in favour of the constant production of a stimulus in the ventricles. Disease in man sometimes performs

definite experiments for us and a few cases have now been recorded where the existence of an independent ventricular rhythm was occasionally manifest, although as a rule the ventricles only contracted in response to the stimulus descending from the auricles (cp. Mackenzie⁷, Wenkebach⁸, Lewis⁶ and probably Joachim⁵). In these cases there was as a rule evidence of some affection of the conductivity between the auricles and ventricles; the ventricles contracted on their own account when the auricular stimulus did not arrive before their own was completely formed. Recorded examples of this dormant ventricular rhythm are very few in number and additional evidence is still required, which encourages me to put on record a case where the existence of an independent ventricular rhythm was very clear.

The patient was a woman, aged 71, who had had eleven children and during the greater part of her life had worked very hard at a machine, continuing to work even during pregnancy and lactation. She had enjoyed good health up to 12 months before she came under observation. Since then she had had attacks of unconsciousness and falling at intervals of two to three weeks. In some of the attacks she had injured herself and she had been informed that she was convulsed during her unconsciousness. The bad attacks commenced with "jumping pain at the lower part of the back and burning in the stomach." Besides these more severe seizures there were numerous slighter attacks in which she merely felt faint without loss of consciousness. Personally I saw one of these faints. The patient drew herself up stiffly in her chair, her face became pale and her expression anxious; by the time I reached her the attack was over so that I was unable to ascertain whether the ventricles ceased beating, or not, during the attack.

On examination the patient was a spare woman, who looked about her age. Nothing abnormal was found in the lungs or abdomen. The arteries were thickened and the pulse tension high (systolic B.P. 200 to 220 mm. Hg.). There was marked visible and palpable pulsation of the carotids. The heart was overlapped by lung; the apex was in the nipple line and was not especially forcible. At the apex a soft systolic bruit could be heard. The cardiac rhythm varied very considerably, the rate being sometimes under 40, sometimes 60 to 65. Intermediate rates were also common and in these the rhythm was always irregular, while in both the more frequent and the more infrequent it was, as a rule, regular as long as they lasted. With the more infrequent rate a soft intermediate sound could generally be heard between the obvious ventricular sounds. This was probably due to the auricular contraction. The urine was acid, the specific gravity was 1010, and there was no albumen.

The patient was admitted into the Westminster Hospital and kept under observation for some weeks. After admission she had only one slight attack, and a few weeks later a more severe one, in which she fell and obtained a bad "black eye." She had noticed previously that if she kept quiet the attacks did not come on, and her second attack occurred the day after her journey to University College to get a tracing with the galvano-

meter. There was considerable improvement in her general health: in fact her only complaints were that her bowels were constipated and that she tended to get flatulence.

A large number of tracings were obtained from her, both before and after admission into the hospital. It was very difficult to get a satisfactory tracing from the jugular: the external jugular pulsated visibly, but, as is frequent, did not give a good tracing. Such as it was, however, the tracing confirmed those obtained below the clavicle. Dr. Mackenzie saw the patient with me and pointed out that there was some pulsation below the right clavicle, and it was found possible to get venous records at this point which were satisfactory. At times when the rate was over 60 a perfectly normal tracing was obtained with the regular sequence of auricle and

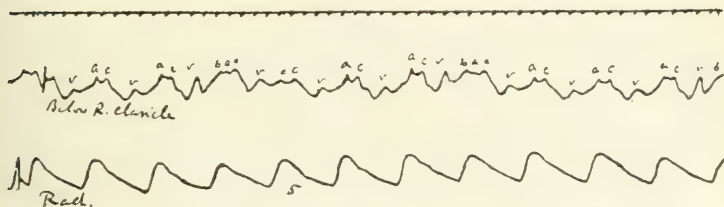


Fig. 1. Auricle and ventricle are beating regularly at the rate of 60 per minute. The A-C interval is about 0.2 sec.. In some places the *b* wave is conspicuous in the venous record.

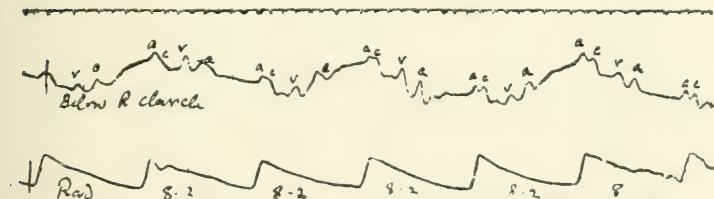


Fig. 2. In this tracing every other beat of the ventricles is dropped out, so that the ventricles are beating at half the rate of the auricles. The auricles are beating regularly at a rate of 73 to 75, and each ventricular systole is preceded by one of the auricles.

ventricle, and with no prolongation of the usual interval between the contraction of auricle and ventricle. Thus, the conductivity of the A-V bundle was apparently in the normal condition. Not infrequently a certain amount of sinus irregularity was present, and occasionally the regularity of the rhythm was disturbed by extrasystoles. These extrasystoles were generally auricular in origin, but sometimes they were ventricular. In

spite of the early occurrence of the auricular extrasystoles there was no appreciable lengthening of the *a-c* interval. In Fig. 2 the ventricles are beating regularly at about 36 per minute, and the venous tracing shows that the auricles are beating at double this rate, so that the record looks as if it had been obtained from an ordinary case of heart-block. A more usual type of tracing showed an intermission of every third beat of the ventricles instead of every second, and in some of these tracings the auricular wave appeared before each ventricular wave as well as in the middle of each long pause. These pauses were often a little shorter than would be expected: that is to say, the long pauses were not quite double the short, but the difference was very slight. The reason of the difference was that the *a-c* interval was slightly shorter after the long pause than after the short, but even after the short pause the interval was only the normal 0.2 of a sec.. This shortening of the *a-c* interval was probably due to an independent early beat of the ventricles and not to a more rapid conduction of the stimulus.

In some of the tracings the intermediate *a* wave, which is associated with a ventricular quiescence, occurs earlier than would be expected, as for instance in Fig. 4. At first I thought that in this tracing the real *a* wave was the smaller one, following the one marked *a* in the record, and that the larger wave was the one described by Gibson² as sometimes being found between the *r* wave and the succeeding *a* wave. This *b* wave, as Gibson calls it, was often conspicuous in this patient before the *a* wave that proceeds a normal ventricular contraction. Some records, however, which were kindly taken for me by Dr. Thomas Lewis with Einthoven's string galvanometer show clearly that the auricular systole, which is unaccompanied by a ventricular contraction, sometimes occurs too early. A similar early occurrence of the blocked *a* wave is also shown in some of the curves obtained by Hay from a case of "Heart-block due to depression of excitability." The explanation of this early *a* wave is difficult: possibly it is a late auricular extrasystole which is blocked, but this does not seem probable. It is, of course, possible that this auricular systole is not really too early but that the next systole of the auricle is too late. Some curves from this patient seem to show that this interpretation may be correct, but it is still more difficult to account for the lateness of the auricular systole succeeding a block than for the early occurrence of an auricular systole just before the block.

Independent ventricular contractions are shown in Fig. 3, where a ventricular beat is dropped out after every third auricular beat; each long pause is ended by a ventricular systole, which occurs before the arrival of the usual stimulus from the auricle, so that auricle and ventricle beat simultaneously. The appearance of the *c* wave in the venous tracing where this occurs is quite different to that of the other *c* waves: the waves are flatter and broader. In some places the *a* wave seems to come distinctly after the *c* wave. The auricles in Fig. 3 are beating at the rate of 66.6 per minute, while the ventricular stimulus is being built up for a rate of 37.5 per



Fig. 3. An example of a 3:2 rhythm, where after the long pause produced by an intermission of the ventricles the independent ventricular rhythm comes into play, so that the ventricular beat occurs at the same time as the auricular or even precedes it.

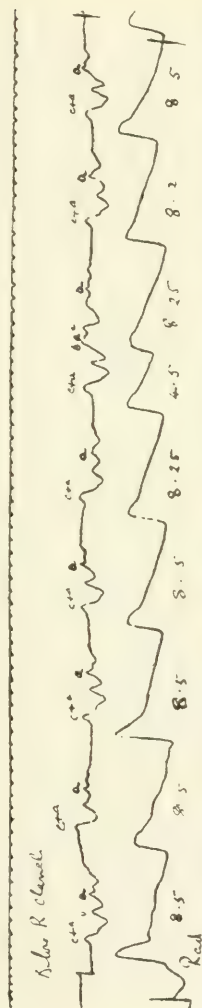


Fig. 4. Shows a temporary complete dissociation of the rhythm of auricle and ventricle. The relation of the rhythm of the auricles to that of the ventricles is as 2:1. The length of the ventricular intervals is such that the independent rhythm of the ventricles can come into play, and the ventricular systole occurs at the same time as the auricular, while the intermediate auricular beat is blocked. Evidently this complete dissociation is started by the sudden change of a 3:2 rhythm into a 2:1, the 3:2 rhythm being of such a character as to allow the independent ventricular rhythm to show itself after the long pauses. In the centre of the tracing there is a momentary return to the 3:2 rhythm, and this occurred again at the end of the record. The interval after the intermediate α wave is markedly longer than that before it. This is most clearly shown after the short ventricular interval in the middle of the tracing.

minute. Hence, whenever a ventricular beat is dropped the next ventricular stimulus would be ready in 1.6 of a sec., whereas the stimulus for the auricles would not be ready until 1.8 of a sec. after the last auricular beat but one. It follows, therefore, that the two contractions should exactly coincide since 0.2 of a sec. is required for the conduction of the stimulus from auricle to ventricle. As explained above it is possible that the auricular wave after a block is sometimes delayed which would bring it just after the *c* wave, thus explaining the broad appearance of these *c* waves and the occasional presence of a distinct double wave.

Sometimes, for a short period, every other ventricular beat was dropped and the auricular beats associated with ventricular ones were found not to precede the ventricular systoles but to occur simultaneously with them, thus producing the appearance of complete heart-block (Fig. 4). Evidently what had happened was that the heart, in which a block was occurring after every third auricular beat, suddenly began to drop every other ventricular beat. The auricles in Fig. 4 are beating at 73, while the ventricles are building up their stimulus for a rate of 36.5. After the long pauses the ventricular rhythm comes into play and the beats of auricles and ventricles coincide. With the establishment of a 2:1 rhythm all the ventricular pauses are long and the ventricles always beat before the arrival of the auricular stimulus. Such complete dissociation only lasted in this case for a very short time either returning as in Fig. 4 to a 3:2 rhythm, or, with an increased auricular rate, to a 2:1 in which the auricles contracted each time before the ventricles. The shortest interval observed before an independent ventricular beat was 1.6 of a sec. (i.e., a ventricular rhythm of 37.5 per minute), but, as a rule, the ventricular rhythm was slower.

In some tracings obtained from the jugular there was an absence of the auricular beat before some of the ventricular ones, and yet the above explanation did not seem to be applicable. For instance, in Fig. 5 in the jugular tracing one finds that, although the ventricles are beating at the rate of 37.5 per minute, and there is apparently a condition of 2:1 heart-block, yet for a considerable period there is a conspicuous *a* wave before every alternate *c* wave and a complete absence of the *a* wave before the others. The intermediate *a* wave, corresponding to the block is here very obscure, though later in the same record, where *a* occurs before every *c*, intermediate *a* waves are often of great size. As the ventricular intervals are all of the same length it is impossible to explain this tracing by supposing that the independent ventricular rhythm asserts itself at every alternate beat: this explanation would necessitate the assumption that there is an extraordinary auricular irregularity of which there is no other evidence. I think that the clue to the correct explanation is afforded by Fig. 6. In this tracing the rhythm is regular and there is no block, but in the jugular the *a* wave is found preceding the *c* wave for two successive beats and then for two successive beats there is no *a* wave and this occurs regularly throughout the tracing. Here the variations in the venous pulse are evidently due to the

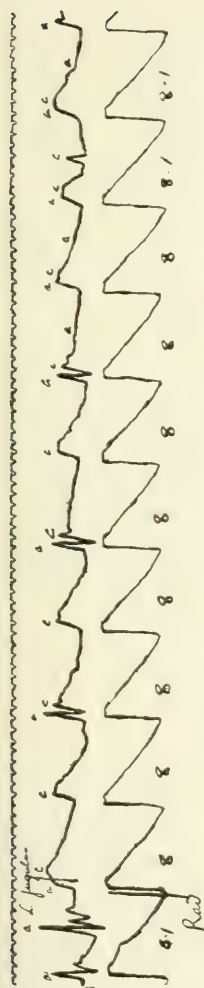


Fig. 5. Shows a tracing obtained from the radial and the left jugular. The rhythm is a 2:1, but there is a curious irregularity in the appearances of the *a* wave. In the first part of the tracing this only comes before every other *c* wave, while at the end it precedes every *c* wave. The intermediate *a* wave is sometimes very conspicuous, sometimes absent. This irregularity is probably due to the influence of respiration, the *a* wave appearing with inspiration and disappearing with expiration.

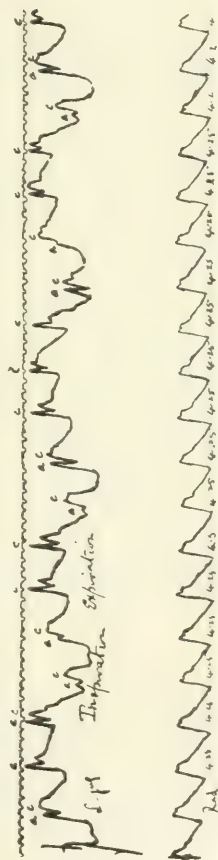


Fig. 6. Shows the influence of the respiratory movements on the pulse in the left jugular. The respiratory movements can be seen in the tracing the curve falling with inspiration and rising with expiration. The *a* wave disappears with expiration and reappears with inspiration.

influence of the respiratory movements, the *a* wave appearing at the end of inspiration and disappearing with expiration, a not uncommon phenomenon in records from jugular veins. On comparing the two tracings, if we suppose that the rate of respiration is the same in Fig. 5 as in Fig. 6, it will be seen that if the presence of an *a* wave in Fig. 5 be taken as corresponding with inspiration the absence of the *a* wave would correspond with expiration. Hence it is more than probable that the peculiar features of this jugular tracing are due partly to the difficulty experienced in getting a satisfactory record from the jugular vein in this case and partly to the influence of the respiratory movements on the tracing obtained.

It has been pointed out already that in these tracings there is no evidence of impairment of conductivity in the bundle which connects the auricles and ventricles, although the stimulus descending from the auricles is frequently blocked, as shown by the ventricular intermissions while the rhythm of the auricles remains regular. In most cases of partial heart-block an impairment of conductivity is definitely shown by a lengthening of the time required for the passage of the stimulus from auricle to ventricle when the ventricle happens to respond to every auricular beat. No such lengthening is found in the tracings from this patient, the *a-c* interval being of the normal length of 0.2 of a sec. in Fig. 1 and elsewhere. So far three other cases of heart-block, without any sign of impairment of conductivity, have been recorded (Hay³, Wenckebach⁴, and Joachim).⁵ Hay and Wenckebach have suggested that in these cases there is deficiency of excitability in the ventricles or in the A-V bundle. It must be remembered, however, that we have no definite sign of the condition of excitability or contractility in the bundle, such as the length of the *a-c* interval affords us as to the condition of the function of conductivity. Thus, the hypothesis that heart-block can occur from deficiency of excitability has not in its favour such conclusive evidence as exists for the more common block from impairment of conductivity.

CONCLUSIONS.

1. There is a constant building up of a stimulus in the ventricles, which stimulus is destroyed by each systole. Given an opportunity this stimulus induces a rhythm in the ventricles at the rate of between 30 and 40 per minute. Under ordinary circumstances this ventricular rhythm is concealed by the more rapid rhythm imposed on the ventricles by the sinus venosus, or what represents the sinus in higher animals.

2. It is possible to get a condition resembling heart-block when the conductivity of the A-V bundle is intact as shown by the length of the *a-c* interval. This may be due to deficiency of excitability in the ventricles as has been supposed by Hay and Wenckebach. It is interesting that in this patient syncopal and epileptic attacks also occurred. Whether these attacks

were associated with cessation of the ventricular beats over a prolonged period, could not be ascertained, though this was probable from the analogy of other cases of heart-block.

3. Heart-block is sometimes accompanied by an irregularity of the auricular rhythm. This shows itself either by a too early occurrence of the beat that is blocked, or as seems probable from this case by a too late occurrence of the succeeding beat. Heineke, Müller, and Höslin¹ found the exact opposite to this in a case, where the auricular beat that was blocked came later than it should.

4. The influence of the respiratory movements must be remembered as a possible cause for the non-appearance of an expected auricular wave in the jugular curve.

BIBLIOGRAPHY.

- ¹ CUSHNY. *Heart*, 1909, i, 1.
- ² GIBSON. *Lancet*, 1907, ii, 1380.
- ³ HAY. *Lancet*, 1906, i, 139.
- ⁴ HEINEKE, MÜLLER and HÖSLIN. *Deutsch. Archiv f. klin. Med.*, 1908, xciii, 459.
- ⁵ JOACHIM. *Berl. klin. Wochenschr.*, 1908, xlv, 911.
- ⁶ LEWIS. *Quart. Journ. Med.*, 1909, ii, 356.
- ⁷ MACKENZIE. *B.M.J.*, 1902, ii, 1411.
- ⁸ V. TABORA. *Zeitschr. f. exper. Path. u. Therap.*, 1906, iii, 499.
- ⁹ WENCKEBACH. *Archiv f. Anat. u. Physiol.*, 1908, Phys. Abth., 53.

NOTE ON THE BLOOD-PRESSURE AND LYMPH FLOW IN A CASE OF HEART DISEASE IN A DOG.

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THE analysis of the factors involved in the production of the conditions associated with states of disease is rendered difficult in many cases by the impossibility of accurately reproducing these states in the lower animals. It is true that, in the case of heart disease, the devices adopted by Bolton (suture of the pericardium or graduated obstruction of the larger venous trunks) have resulted in the production of some of the morbid conditions generally associated with heart disease and especially with the production of hydrothorax, œdema of the mediastinum and ascites. It might be asserted, however, that these conditions are not strictly comparable to the state of chronic heart failure which is present in heart disease, whether due primarily to alteration in the valvular orifices or to changes in the heart muscle. In man we are able at the present time to measure arterial pressures, but our views on the lymph production and lymph flow in failure of compensation are naturally still matters of surmise. It therefore seems to us of interest to put on record the following observations on a dog with chronic heart failure.

The dog was a small mongrel fox-terrier weighing after bleeding and loss of ascitic fluid $6\frac{1}{2}$ kilos. It had suffered from increasing weakness, wasting and ascites for the last three months. It was not thoroughly examined until it had received a dose of morphia ($\frac{1}{4}$ grain), and had been anæsthetised with A C E mixture and secured on the operating table. It was noted that the abdomen was largely distended with fluid, but that the rest of the body was emaciated. The heart impulse was diffuse but no definite bruit could be detected on auscultation. The pulse was regular, no enlargement of the liver could be made out. Post mortem both sides of the heart were found to be dilated without any compensatory hypertrophy. The edges of the tricuspid and mitral valves were thickened, but there seemed no condition other than the weakness of the cardiac muscle which would have caused any regurgitation through these orifices. The liver presented the typical appearance of non-compensation, the capillaries in the interior of the lobules being widely dilated with a thinning of the intervening trabeculae of liver cells. The spleen was tough and fibrous

with old cicatrized infarcts. The kidneys were hard, but presented the normal relation between cortex and medulla. No degenerative changes in the kidney were to be seen on microscopic section. The abdomen contained 2310 cc. of ascitic fluid, the right pleura 125 cc., and the left pleura 90 cc. pleural fluid. There was no oedema of the extremities or subcutaneous tissue. No morbid conditions were present in the peritoneum, so that the dropsy must be regarded as due entirely to the heart failure. The results therefore can be regarded as due entirely to the cardiac condition.

Cannulæ were placed in the thoracic duct, in the carotid artery for registration of blood-pressure, in the femoral vein, $1\frac{1}{2}$ inches below Poupart's ligament, and in the jugular vein at the angle of the jaw for measuring the venous pressures. The following table shows the lymph flow and the pressures at different periods of the observation.

| Time. | Lymph Flow (Blood-stained). |
|----------|-----------------------------|
| 10.40-50 | 30 cc. |
| 10.50-60 | 21 cc. |
| 11. 0-10 | 17 cc. |
| 11.10-20 | 12 cc. |
| 11.20-30 | 11 cc. |

The pressures during this time were as follows:—

| | |
|------------------------|--|
| Mean arterial pressure | 90 mm. Hg. |
| Jugular vein | 30-45 mm. Na_2SO_4 * |
| Femoral vein | 150-160 mm. Na_2SO_4 . |

The normal respiratory undulations in the volume of the jugular vein were absent, the vein remaining expanded during inspiration as well as expiration. In the normal animal the jugular vein at the base of the neck collapses during inspiration. The abdominal pressure as measured through a trochar plunged into the peritoneal cavity was 100 mm. Na_2SO_4 . The fluid was then allowed to run out of the abdominal cavity. During the next 30 minutes the emptying of the abdominal cavity was assisted by manipulation, so that the lymph flow during this time cannot be regarded as normal.

| Time. | Lymph Flow. |
|----------|------------------------------------|
| 11.30-40 | 11 cc. (Abd. pressure on and off). |
| 11.40-50 | 14 cc. " " " |
| 11.50-60 | 20 cc. " continuous). |

The abdomen being now empty the pressures were once more measured, and were as follows: carotid artery 100 mm. Hg., jugular vein, 20 mm. Na_2SO_4 (the vein collapsing now with each inspiration), femoral vein, 70 mm. Na_2SO_4 . The pressures were thus practically normal, as may be seen by comparing them with those taken the next day by one of us (C. Bolton) on a normal

* Na_2SO_4 stands for a half saturated solution of sodium sulphate. 12 mm. Na_2SO_4 may be taken as roughly equivalent to 1 mm. Hg..

dog weighing 6.3 kilos. The pressures in the normal dog were :—carotid artery, 95 mm. Hg., jugular vein, 28 to 38 mm. Na_2SO_4 (collapsing with each inspiration), femoral vein ($1\frac{1}{2}$ inches below Poupart's ligament), 85 mm. Na_2SO_4 . The lymph flow in this normal dog, which can be regarded as an average quantity, was as follows :—

| Time. | Lymph Flow. |
|----------|-------------|
| 11.10-20 | 3.25 cc. |
| 11.20-30 | 2 cc. |
| 11.30-40 | 2 cc. |
| 11.40-50 | 2 cc. |
| 11.50-60 | 1.35 cc. |
| 12. 0-10 | 1.8 cc. |
| 12.10-20 | 2.5 cc. |

Although the pressures had returned to normal in the dog with heart disease there was no diminution in the lymph flow, as will be seen from the following record :—

| Time. | Lymph Flow. |
|----------|-------------|
| 12. 0-10 | 16 cc. |
| 12.10-20 | 15 cc. |
| 12.20-30 | 16.5 cc. |
| 12.30-40 | 14 cc. |
| 12.40-50 | 13 cc. |
| 12.50-60 | 12.5 cc. |
| 1. 0-10 | 11 cc. |
| 1.10-20 | 10.5 cc. |
| 1.20-30 | 11 cc. |
| 1.30-40 | 11.5 cc. |
| 1.40-50 | 11 cc. |
| 1.50-60 | 13 cc. |
| 2. 0-10 | 11 cc. |

At 2.15 the dog was killed by bleeding. Unfortunately we did not measure the whole quantity of blood by washing out the vessels. Since, however, 500 cc. of blood were obtained by simply bleeding there was evidently a condition of plethora present. In the normal dog mentioned above 300 cc. were all that could be obtained without washing out the vessels, and this is the amount that one expects to get from any normal animal of the same size. Examination of the fluids obtained from the dog with heart disease gave the following results :—

| | Total Solids. | Freezing Point. |
|-------------------------|----------------|-----------------|
| Blood serum .. | 7.71 per cent. | —0.52 C. |
| Peritoneal Fluid .. | 6.18 .. | —0.515 C. |
| Pleural Fluid .. | 5.16 .. | —0.515 C. |
| Lymph before tapping .. | 5.69 .. | —0.55 C. |
| Lymph after tapping .. | — | —0.62 C. |

DISCUSSION AND CONCLUSIONS.

Among the results obtained the following are worthy of note:—

1. As has been shown in cases of heart disease in man the arterial pressure in the animal at rest practically corresponds to that in a normal animal. Chronic heart failure does not involve a lowering of arterial pressure.

2. Although the venous pressures were somewhat raised, the rise in the jugular vein was minimal, while that in the femoral vein was chiefly conditioned by the pressure of the ascitic fluid on the inferior cava. On removal of this fluid the pressures became normal. The only important difference between this animal and a normal animal was found in the absence of the negative pressure during inspiration, so that at all phases of respiration there was probably slight positive pressure in the big veins of the heart. These results are in accordance with those obtained by Bolton in his experiments on artificial constriction of the large venous trunks.

3. The amount of circulating blood was certainly increased, i.e., a condition of plethora was present. The presence of plethora in these cases was predicted by one of us on theoretical grounds many years ago, and has since been confirmed by Haldane's method in various cases of heart disease in man¹.

4. In the same publication it was shown that even a slight rise of venous pressure in the inferior cava near the heart, especially if associated with stagnation of the blood, would tend to produce increased lymph production from the vessels of the liver, and therefore an increased flow of lymph from the thoracic duct. The large but rapidly decreasing lymph flow obtained on first inserting a cannula into the thoracic duct seems to indicate that there was a definite obstruction to the emptying of lymph into the venous system, for which the absence of the normal negative inspiratory venous pressure may probably be held responsible. Towards the close of the observation, however, the venous pressures were normal, while the lymph flow remained at a height three to four times as large as that obtained from a normal animal. We are not in a position to say whether this increased flow was an index of increased lymph production, and therefore of some change in the blood vessels leading to abnormal permeability, or whether it was due to a continued draining off of lymph from the lymph spaces which had been over-filled during the previous condition of ascites.

Experiments on the production of pleural effusion² have shown that in all probability the primary seat of this production is in the tissues of the mediastinum. It is worthy of note that directly the carotid sheath was opened, and with it the posterior mediastinal tissues, for the purpose of exposing the thoracic duct, these tissues were found to be cedematous, fluid welling up in the bottom of the wound.

5. Although during the course of the observation 250 cc. of lymph were withdrawn from the animal the arterial blood-pressure continually improved, rising from 90 mm. Hg. at the beginning of the observation to 110 mm. Hg. just before the animal was killed. It is probable that the withdrawal of fluid from the lymphatic system acted very much as a moderate bleeding would under the same conditions, and by a diminution of the total volume of the circulating blood served to relieve the distension at the venous end of the heart, so enabling it to beat more effectively.

In consequence of the rarity of these cases we have thought it worth while to put this isolated case on record. We hope, however, that we shall have further opportunities of investigating similar cases and of clearing up many points which still remain obscure.

BIBLIOGRAPHY.

- ¹ BOLTON. *Journ. of Pathol. and Bacteriol.*, 1909, XIV, 49.
- ² LEATHES and STARLING. *Journ. of Pathol. and Bacteriol.*, 1895, IV, 175.
- ³ STARLING. *Lancet*, 1896 (Arris and Gale lectures, Lecture III). See also "The Fluids of the Body" (Constable, 1909, 150).
- ⁴ LORRAIN SMITH. *Trans. Path. Soc.*, 1902, LIII, 136.

SINUS ARRHYTHMIA, ASSOCIATED WITH ANGINAL ATTACKS OF A VASO-MOTOR TYPE.

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WE are accustomed to think of sinus arrhythmia as an irregularity belonging to childhood and early adult life. The mechanism in this example of disordered cardiac rhythm was first considered and carefully described by Mackenzie¹ under the title of "Youthful irregularity." It is of very common occurrence in children at or about the age of puberty, when the pulse finally decreases in rate and assumes the rhythm which persists during the remainder of adult life. As a rule it is definitely related to respiration. In those who manifest it, the long pauses occur with the natural expirations, the quickening with inspiration. In the adult, there is commonly no trace of alteration in the frequency of the pulse during quiet respiration, but with forced or laboured breathing, alterations of rhythm are well known to occur. In dogs, respiratory irregularity is the rule, and is well marked even when the animals are asleep. Both in the human subject and in the lower animals, the irregularity of rhythm is universally attributed to waxing and waning of vagal tone, for it is completely abolished by section of the vagi in the latter. In the healthy adult, these disturbances of pulse frequency are practically unknown in a marked form, but as Mackenzie stated, they are not uncommon subsequent to febrile attacks or in adults upon recovery from broken compensation.

The sinus irregularity which is here described is, so far as I know, almost unique in its grade: it is associated with slow action of the heart and with frequent attacks of an anginal nature. I am indebted to Dr. Sidney Martin for opportunities to investigate the case and for permission to place it on record, and to Dr. Lewis for the curves and their interpretation.

HISTORY. ETC.

H. M., aged 36, a companion and a single woman, was admitted to University College Hospital on 20th April, 1909, for observation upon the condition of her heart. She had large fibroids of the uterus associated with irregular catamenia and considerable uterine pain. The main purpose of

her stay in hospital was to ascertain the desirability of operative interference with these tumours.

The family history is of little interest. The father died of heart failure, and the mother of consumption. Her two brothers are both dead of causes unknown; there were no sisters.

Previous History.—At 10 years of age she had rheumatic fever, and when 12 years old typhoid fever. One year ago she was laid up with pleurisy. In habits she has been quite temperate; her social condition is good, her work light, but the hours of work long.

The present illness.—Her present symptoms have been of ten years' duration, and during that time she has suffered from attacks of pain in the left side of the chest, associated with severe palpitation and faintness. The pain starts in the precordial region and radiates from this situation to the left shoulder, down the inner side of the upper arm, extending down and across to the radial side, into the thumb and adjacent fingers. The pain is associated with considerable anxiety and distress, and a sensation of constriction in the chest and inability to draw the breath. At times, and in the severer attacks, the radiation is more extensive, both sides of the neck are affected and also the right side of the chest. The pains are only acute during the attack, but soreness persists and is accompanied by hyper-sensitiveness of the corresponding areas of skin for 24 to 36 hours subsequently. Numbness and tingling of the fingers of the left hand are almost continuously present. The attacks are very frequent but variable in their occurrence; thus there may be intervals of weeks or months over which none are experienced, while at other times they succeed each other within seven, four or even two days. They usually start in the evening and are of about 10 minutes' duration; they vary greatly in intensity. She does not think that they have been more frequent of late, and knows of no definite cause to which to attribute them. She has noticed that her hands become white and insensitive directly before and during the attacks. She recognises their imminence by this means and by a general sense of uneasiness and distress which may be present for some little while prior to the onset of the more severe symptoms.

Condition.—The general impression conveyed upon examination was that of a patient with a delicate constitution, and an excitable temperament. She was comfortable and in no distress. There were no signs of broken compensation. The pulse was slow (45 to the minute), and markedly irregular: the arteries were slightly sclerosed and the tension somewhat raised (S. B. P. 150 mm. Hg.*). The heart's apex beat was in the fifth interspace, 4 inches from the midsternal line. The left limit of cardiac dulness was 4 inches, the right limit 0 inches from the same point. The cardiac sounds were clear and loud, and at the apex a blowing systolic murmur was present. The lungs were free from abnormal physical signs. Abdominal and pelvic examination confirmed the diagnosis of uterine fibroids. The urine was normal and nothing was detected in the nervous system.

* Reading with Martin's modification of Riva Rocci's instrument.

SPECIAL EXAMINATION OF THE HEART.

Numerous polygraph curves were obtained and are illustrated by the accompanying figures.

The irregularity as it presented itself at first is illustrated by Fig. 3, and consists of short and long beats placed in haphazard relation to each other. Measurements of the beats show that where a long pause succeeds more than one shorter pause, the length of the longer pause is approximately or actually double that of the pause directly preceding it. This is shown in two places in the figure. Beats which succeed the longer pauses are invariably somewhat increased in length as compared to the shorter beats already referred to.

The tracing was taken during a period of suspended breathing. On most subsequent occasions when curves were taken, the irregularity showed a definite relationship to respiration, but otherwise exhibited much the same characteristics. An example is given in Fig. 1, and the tracing includes a simultaneous respiratory curve. To the left the breathing is natural, and near the summit of each inspiration a shortened pause occurs. With forced breathing, as seen in the last part of the same figure, the irregularity maintains its relationship to the breathing, but is much more marked. While the relationship to respiration was beyond question, it was not invariably a pure respiratory arrhythmia: thus Fig. 2 shows two phases of more rapid pulsation, and, on the suspension of breathing, the heart becomes regular and slow; but at one point a shortened pause disturbs the otherwise almost regular rhythm. The same relationship to respiration is depicted in Fig. 4, in which the long pauses occur at every third beat.

In Fig. 5 they are present at every fourth beat, and in these two figures, the relationship of the length of the long beat to the length of the short beat directly preceding it, or to the two short beats in the case of Fig. 5, is very striking. In both these curves, too, the beat succeeding the lengthened pause is invariably increased in length.

The mechanism, so far as it has been examined, appears to consist of a normal rhythm intercepted by longer pauses of variable frequency in their incidence. On rare occasions, long intervals occur, over which long pauses alone are met with. An example is given in Fig. 6, where the pulse rate is approximately 39 per minute. At other times with natural breathing, the pauses in the radial pulse are of very irregular length, and the longest (Fig. 7) show no relationship to the preceding pauses. At the same time, a similar general type of irregularity is present, for each of the notably long pauses is succeeded by two or more beats of a rhythm in which the rate is gradually increasing. It is apparent that we are dealing with an arrhythmia of a very definite type, but which is complicated by more than one factor. It is an irregularity in which auricle and ventricle always participate to a like extent, for each beat of the ventricle is preceded by an auricular wave, *a*.

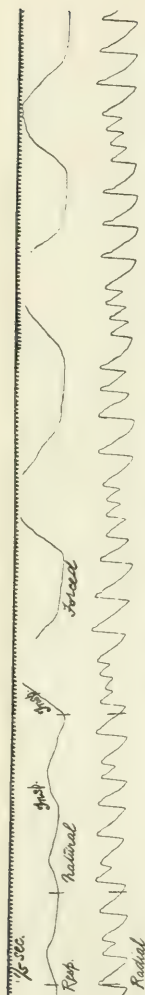


Fig. 1. $\times \frac{1}{4}$ linear. Respiratory curve and radial pulse. Natural and forced breathing. The tracing shows the dependence of the arrhythmia upon respiratory reflexes. The short pauses fall with inspiration, the long with expiration and the pause.

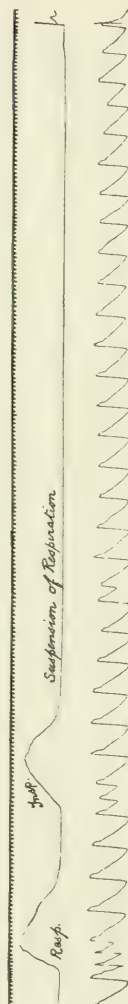


Fig. 2. $\times \frac{1}{4}$ linear. Respiratory curve and radial pulse. During natural breathing and during a suspension of respiration; a single short pause interrupts the last period.

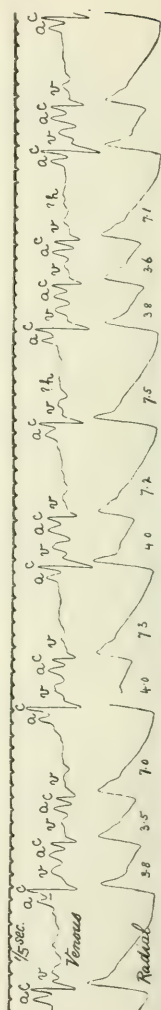


Fig. 3. $\times \frac{1}{4}$ linear. Venous and radial curves showing the analysis of the heart's mechanism. Each beat is accompanied by a , c , and v waves. Breath held. The long pauses occur after one, two, or three beats.

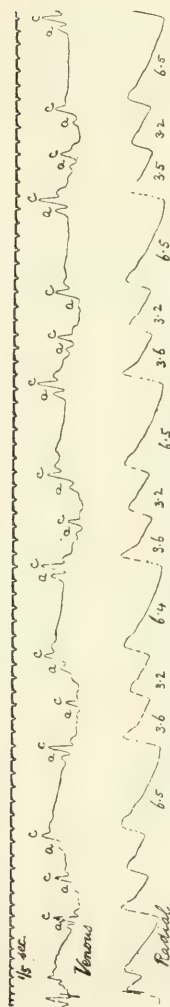


Fig. 4. γ γ γ linear. The same, showing a respiratory relationship. The pauses occur regularly after 3 beats. As in the last two figures there are definite numerical relationships between the lengths of the beats.

in the jugular pulse. Cardiograms show no trace of any beats other than those depicted, and a precisely similar observation applies to long electrocardiographic curves which were also obtained. The question which first offers itself for discussion is the nature of the long pauses, treated individually. The definite relationship of the lengths of these pauses to those of preceding beats is so frequent and so constant, as to suggest the presence of a sino-auricular block, such as has been recorded as the interpretation of an irregularity by Wenckebach³.

In examples, such as those shown in Figs. 3, 4 and 5, such an explanation would suffice. The increased length of those beats which directly succeed the longest pauses* may be due to a shortening of the preceding Ss-As interval. In examples, such as that shown in Fig. 7, the interpretation will not hold, and curves of this nature convey a doubt as to whether we are justified in assuming sino-auricular block, even in clear instances where in an otherwise regular rhythm an occasional dropped beat is present, auricle and ventricle participating.

We cannot escape the conclusion that the mechanism in this instance is the result of alterations of vagal tone, for the irregularity is usually entirely subservient to respiration. This in itself would not exclude the possibility of a depression of sino-auricular conductivity as a basal factor in the mechanism of production of the long pauses. At times, as we have seen, the irregularity may occur in the absence of breathing; this likewise does not exclude the vagus as the cause of the varying lengths of the beats. A direct test was therefore attempted soon after the admission of the patient and at a time when the pulse rate lay consistently between 40 and 52 per minute; belladonna was given in doses of 5 minims of the tincture at intervals of 4 hours, and was steadily increased during the next few days until a dosage of half a drachm was reached. Further than this the dose could not be carried, as the drug distressed the patient. But, though the long pauses were never absent at any time, yet the pulse rate increased at frequent intervals to rates of 80 and 100, and such rates had never been met with during the first five days of observation, when no drugs were employed.

The conclusion, therefore, seems to be that the doses of atropine administered were distinctly influential in cutting down the frequency of the long pauses responsible for the usual slow pulse rate; and the observation supplies confirmatory evidence that the arrhythmia as a whole was of vagal origin.

ATTACKS OF ANGINA PECTORIS.

While in hospital the patient experienced several attacks of angina pectoris, and the account of her symptoms previously given was confirmed. Seen in several of them, the following observations were made:—The earliest

* A similar phenomenon is well seen in a parallel and experimental irregularity recorded by Hering (*Zeitschr. f. exper. Pathol. u. Therap.*, 1906, III, Fig. 3 K).

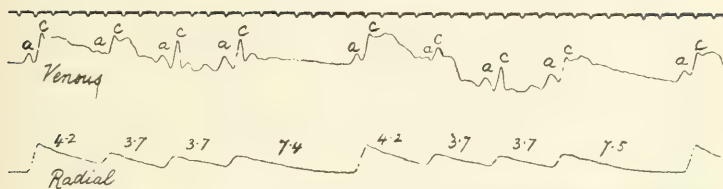


Fig. 5. $\frac{1}{5}$ linear. The same; the long pauses occur at each fourth beat. Numerical relationships are very exact.

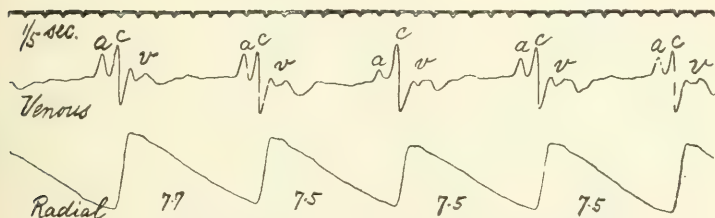


Fig. 6. A curve consisting of long beats only; suspended respiration.

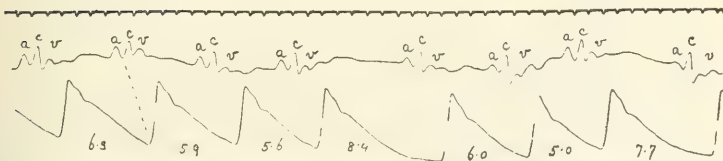


Fig. 7. $\frac{1}{5}$ linear. An example of an arrhythmia occasionally shown. The lengths of pauses show no definite numerical relationship.

sign of onset was the blanching of the face and extremities, and it was accompanied by great precordial distress and urgent dyspnœa. With the increasing distress the patient often became speechless and rigid, clutching to the sides of the bed for support. The expression was anxious, the pulse rate was invariably markedly increased, rising to 110 or 146. The pulse was sometimes irregular at these rates; but no tracings were obtained at such times. As a rule, the rate was maintained until the end of the attack; on one occasion it was not sustained. As the attack proceeded, slight cyanosis of the lips was manifest and the extremities became cold and clammy. Blood pressure observations during many of the attacks showed constant results*. Three series of observations, the most perfect, are included in the accompanying table:—

First attack (6th June).

| Time. | | Blood-pressure. | Pulse. |
|-----------|-------|-----------------|--------|
| 7. 0 p.m. | | 114 | 44 |
| 9.20 .. | onset | 114 | 10 |
| 9.23 .. | | 154 | 68 |
| 9.26 .. | | 150 | 68 |
| 9.31 .. | | 150 | 68 |
| 9.37 .. | | 142 | 50 |
| 10. 0 .. | | 140 | 52 |
| 10.15 .. | | 130 | 40 |
| 11. 0 .. | | 130 | 44 |

Second attack (12th June).

| | | | |
|-----------|-----------------------|-----|-----|
| 7. 0 p.m. | | 130 | 56 |
| 9.10 .. | (shortly after onset) | 170 | 132 |
| 9.15 .. | | 170 | 140 |
| 9.20 .. | | 130 | 60 |
| 9.35 .. | | 120 | 52 |
| 10. 0 .. | | 120 | 56 |

Third attack (14th July).

| | | | |
|-----------|---------|-----|-----|
| 7. 0 p.m. | | 130 | 46 |
| 10.22 .. | (onset) | 130 | 124 |
| 10.25 .. | | 164 | 146 |
| 10.28 .. | | 168 | 140 |
| 10.31 .. | | 168 | 72 |
| 10.34 .. | | 124 | 50 |
| 10.45 .. | | 124 | 54 |
| 11. 0 .. | | 120 | 54 |

From the usual S. B. P. of 110 to 130, a sudden rise to 150, 160 or 170 was an invariable accompaniment of the angina. With the offset of the attack, the increased pulse rate and B.P. gradually subsided, and the patient lay in a semi-collapsed state, shivering violently. The temperature was never raised. Subsequent to the attack, exhaustion and headache were frequent.

* The rise of blood-pressure was not the result of the rigidity before mentioned. The limbs were relaxed at the times when the observations were made.

Cutaneous tenderness was almost universal, but was specially marked over the left chest, in the neck, down the inner surface of the left upper arm and the radial border of the same forearm. Deep tenderness was also noted in the pectorals and deltoid of the left side. Pressure in the intercostal spaces in the left axilla could not be borne, and frequently the sterno-mastoids were too sensitive to allow the application of the polygraph receiver. Otherwise nothing abnormal was noted. The heart was never dilated during the attack, the percussion limits being identical with those preceding it.

The patient has more recently submitted to operation, in which a partial hysterectomy was performed. Subsequent to the operation, the pulse was frequent and regular for long intervals and for several days. As a rule, in long strips of curve, only occasional pauses were recorded. The length of a pause was always exactly double that separating two normal beats. During the whole of this time the patient complained in a minor degree of precordial anxiety and of tenderness of the skin areas. On one or two occasions definite anginal attacks occurred. Later, these subsided and the original pulse irregularity returned.

DISCUSSION.

The symptomatology of the attacks shows many points of resemblance to the original symptom-complex described by Nothnagel.² The radiating pains so characteristic of cardiac seizures form a prominent feature of this case. The nature and distribution of the pain and its accompanying symptoms is in every way similar to that of so-called true angina pectoris. The disturbances in the extremities point definitely to vaso-motor changes as a cause of the rise of blood pressure, but that this increase of blood pressure was not necessarily the cause of the attacks is shown by the fact that the patient was well aware of her danger before the rise of pressure took place. It is possible, therefore, that in this instance it was rather the result than the cause of the seizure, or that pain and augmented pressure arose from a common cause. The increase of pulse rate during the attacks may be attributed to an abeyance of that increased vagal tone to which has been assigned the customary diminution of heart rate.

It is the possible or probable association of central nervous disturbances conducted along two separate paths, vaso-motor and inhibitory, which gives this case its special interest. It is impossible to assert definitely in what way they are related one to the other, or to the underlying cardiac condition previously described.

BIBLIOGRAPHY.

¹ MACKENZIE. *The Study of the Pulse*, Lond. and Edin., 1902.

² NOTHNAGEL. *Deutsch. Archiv f. klin. Med.*, 1867, III, 309.

³ WENCKEBACH. *Archiv f. Anat. u. Physiol.*, 1906, Phys. Abth., 297.

AURICULAR FIBRILLATION AND ITS RELATIONSHIP TO CLINICAL IRREGULARITY OF THE HEART.*

BY THOMAS LEWIS.

(From the Research Laboratories, University College Hospital Medical School.)

CONTENTS.

| | PAGE |
|---|------|
| HISTORICAL AND INTRODUCTORY | 307 |
| A GENERAL ACCOUNT OF COMPLETE IRREGULARITY OF THE HEART .. | 310 |
| <i>Frequency</i> | 310 |
| <i>Etiology</i> | 311 |
| <i>The symptoms</i> | 312 |
| <i>The radial pulse curves</i> | 314 |
| <i>The venous pulse curves</i> | 316 |
| <i>Certain waves which occur in diastole</i> | 321 |
| <i>The electrocardiographic curves obtained by leads from the right arm and left leg</i> | 325 |
| COMPLETE IRREGULARITY OF THE HEART IS THE RESULT OF AURICULAR FIBRILLATION | 327 |
| <i>The irregular oscillations seen upon galvanometric curves are due to an inco-ordinate contraction of some portion of the heart ; they are not a direct result of structural change in the heart, and are independent of movements of the somatic mus- culature</i> | 327 |
| <i>The irregular oscillations arise in the vicinity of the auricle ; the ventricular electric complex in complete irregularity is of the normal form</i> | 331 |
| <i>Certain deductions from the clinical findings</i> | 333 |

* The expenses connected with this work have been largely defrayed by grants from the Royal Society and the British Medical Association.

| | PAGE |
|---|------|
| <i>Oscillations similar to those characterising complete irregularity of the heart in man are found experimentally when the auricle is fibrillating, and these oscillations are produced in the auricle as a result of the fibrillation</i> | 334 |
| <i>The electrocardiographic curves compared in more detail</i> .. | 337 |
| <i>The radial curves compared</i> | 339 |
| <i>The venous curves and their comparison</i> | 340 |
| <i>A summary of the comparison instituted between the records obtained in complete irregularity of the heart in man, and in experimental auricular fibrillation</i> | 345 |
| AURICULAR FIBRILLATION AS A CLINICAL ENTITY | 346 |
| AURICULAR FIBRILLATION AND HEART BLOCK: THE ACTION OF DIGITALIS | 349 |
| THE CAUSE OF THE ONSET AND DURATION OF AURICULAR FIBRILLATION | 353 |
| AURICULAR FIBRILLATION AND VENTRICULAR EXTRASYSTOLES .. | 356 |
| CERTAIN CONDITIONS DIFFERENTIATED | 357 |
| <i>Cases in which the ventricular form of venous pulse occurs, but in which either auricular fibrillation is absent or in which the evidence is insufficient to justify us in assuming its presence</i> | 357 |
| <i>True "nodal rhythm" is a rare affection and gives rise to a clinical picture entirely at variance with that of the disorderly action of the heart hitherto considered</i> | 360 |
| CHIEF CONCLUSIONS | 368 |
| BIBLIOGRAPHY | 369 |

HISTORICAL AND INTRODUCTORY.

IN the following pages an account of a specific clinical condition, characterised in the great majority of cases by complete irregularity of the arterial pulse and by an absence of all signs of the normal auricular contraction, is given.

It will be shown that the type of irregularity, which is one of the chief features of the condition, is the commonest persistent irregularity exhibited by the human heart, constituting as it does approximately 50 per cent. of all such cases; and it will be demonstrated that the disturbance of cardiac rhythm is to be sought in the auricle and attributed to temporary or permanent inco-ordination of the musculature of that chamber.

In brief, evidence is forthcoming that of the numerous examples of persistent irregularity of the heart familiar to clinicians, approximately 50 per cent. are the result of auricular delirium or fibrillation.*

Our acquaintance with the facts upon which this final conclusion rests is the outcome of the studies of a large body of workers. A retrospective survey of the observations upon clinical material permits the recognition of cases, belonging to the category discussed, over a period of many years. Fully possessed of the facts, we may trace the earlier descriptions of the condition along two lines: and it is mainly upon these separate paths that the course of observation has been pursued, and pursued until quite recent years by distinct investigators. The earliest graphic observations were carried out independently upon the arterial and venous systems. The two paths have converged and finally have met during the last decade. For this union of the facts derived from two separate sources and for the wide range of supplementary knowledge relating to the condition, we are indebted almost exclusively to the introduction of the new graphic methods of examining the cardiac mechanism which are now at our disposal.

On the one hand a markedly irregular pulse, especially associated with mitral disease in its later stages, was the subject of study by mechanical means from the epoch marked by the introduction of the sphygmograph. It is portrayed by Marey¹¹, Riegel^{12b}, Sommerbrodt¹³ and many other writers. It has been termed the "mitral pulse," and has been attributed amongst other causes to "delirium of the heart." It has passed by the name of *Pulsus arrhythmicus* (Janowski^{12c}), and by the name *Pulsus irregularis* (Riegel^{12b}). It has been identified, in a classic but obsolete nomenclature, with the adjectives *irregularis*, *inaequalis*, *deficiens* and *intermittens*.

On the other hand, a prominent systolic pulsation in the veins of the neck was described by Bamberger¹, Skoda^{5a} and others, and was attributed, and has long since been held as due, to tricuspid incompetence. The subjective timing of the venous pulsation was endorsed by Riegel^{12b}, who obtained the first graphic records of the movement: but the class of case in which such pulsation is found essentially was not isolated, neither was its full significance grasped, until the more exact and more applicable technique of Mackenzie was introduced.

It is since the year 1902, when the "Study of the Pulse" was published, that chief progress has been made. It is to Mackenzie that we owe the definite co-relation of the two phenomena, gross irregularity of the heart and the systolic venous movement, which he has termed the "ventricular form of venous pulse." In the work referred to¹⁴, this writer first demonstrated their frequent association and ascribed them both to a single underlying condition, namely, paralysis of the auricle. A year later Hering¹⁵, describing

* Preliminary notices of the observations have appeared^{11a, 12}, and examples of the curves were demonstrated before the Medical Society of London on 13th December, 1909, and before the Pathological Section of the Royal Society of Medicine on 4th January, 1910, at University College Medical School.

the arterial pulse alone, laid more stress upon its characteristics and spoke of it under the title *pulsus irregularis perpetuus**. He appears to claim¹⁷ to have implied, by the use of this term, a specific type of rhythm, but the facts brought forward in his paper failed to carry conviction of an irregularity *sui generis*. The recognition of its specificity has been arrived at gradually and the facts supporting the conclusion have been contributed largely by Mackenzie. In particular, the emphasis which he laid upon its frequent association with the ventricular form of venous pulse in 1904¹⁵, and the prominence given to this observation in a later paper, based upon an examination of 500 cases¹⁷, must be noticed. But in reality it is only since the galvanometric examination of the heart has been available that the probability of its specific nature has grown to certainty.

In his papers of 1904-5, Mackenzie^{15 & 16} brought forward several new and important facts, and most striking amongst them, in the light of our present knowledge, were evidences that the auricle is active. Formerly regarding the auricle as paralysed, because no sign of activity could be found, he attempted at this time to separate a special group of cases in which auricular activity was considered probable. Auricular activity was assumed, (1) because the auricle was found hypertrophied at autopsy; and (2) because certain instances were observed in which the normal rhythm reasserted itself. It is to these papers more especially that we are indebted for the observation that in all cases of complete irregularity of the heart there is an entire failure of signs of the *normal* auricular contraction during diastole; and further, for the first record of cases of this nature, in which it is probable that little dilatation of the right heart and little tricuspid regurgitation is present. His earlier view that the condition results from auricular distension as a consequence of valve incompetence was at least partially abandoned, and the rhythm was ascribed as the cause rather than the result of the eventual dilatation. In 1904 Mackenzie postulated the view which he has since held, that in many cases the seat of the rhythm is in the junctional fibres lying between auricle and ventricle, and by conceiving the simultaneous contraction of auricle and ventricle in response to impulses from this single source attempted to explain the absence of every sign of normal auricular contraction which he had demonstrated to be one of the chief features of such cases. In 1906 Hering¹⁰ realised the correctness of Mackenzie's assertion that the completely irregular pulse when once established is not of necessity perpetual. In 1907 Theopold¹² described cases confirming the view that the rhythm is not a secondary phenomenon to tricuspid leakage.

In 1907-8 Mackenzie¹⁸ adopted the hypothesis of the nodal origin of the rhythm more generally, holding the node of Tawara† to be the seat of

* The qualification "perpetual" has since been discarded.

† A specially differentiated structure at the auricular side of the junctional tissues between auricle and ventricle.

disturbance in all cases of complete irregularity found in combination with the systolic form of venous pulse. He therefore included all such cases under the term "nodal rhythm."*

Hering¹⁵ has recently added evidence of the supraventricular formation of the ventricular impulses.

Such is the history of the main steps in the attempt to unravel the problem of the mechanism upon which the symptomatology is dependent, and, for the time being, this brief account will suffice. Papers relating to the subject have been prolific, a mass of detailed knowledge has accumulated, discussion has been unrestrained and speculation has oftentimes exceeded the limit warranted by the facts. Further reference to the work of previous observers will be made more conveniently under the various headings and sub-headings which follow.

A GENERAL ACCOUNT OF COMPLETE IRREGULARITY OF THE HEART.

The following account of the condition is based upon a close study of seventy-three cases from all of which simultaneous radial and venous curves, and from thirty of which electrocardiographic curves, have been taken. The clinical polygraph and Mackenzie's ink polygraph, fitted with specially light writing points and arranged with a considerable reduction in the air content of the transmission apparatus, have been employed in obtaining records of pulsating areas. The electrocardiograms have been obtained with Edelmann's large pattern of the string galvanometer of Einthoven. During the earlier days when the work was in progress, the electrodes consisted of baths of salt solution in which zinc terminals were immersed, but the greater part of the investigation has been carried out with non-polarisable electrodes consisting of zinc rods immersed in saturated zinc sulphate solution, the last held in a porous jar itself lying in the salt solution. Simultaneous radial or venous and electrocardiographic curves have been secured by adding parts of the Mackenzie polygraph to the galvanometric outfit. The patients were always in the same room with the apparatus while the records were taken.

Frequency.

Complete irregularity of the heart is a very common condition. During two years of observation 114† cases of persistent‡ irregularity of the heart

* On the Continent the rhythm is variously described as "chronic arrhythmia," "arrhythmia perpetua," etc.

† I have excluded entirely all cases of irregularity which I have seen since the first announcement of my view of the mechanism present in complete irregularity of the heart. For since that date I am unable to affirm that the cases presenting themselves have been impartially chosen. It is on this account that the number of cases of complete irregularity from which the conclusions as to the mechanism are drawn exceed those mentioned in the statistical account which is now given.

‡ By persistent irregularity I denote cases in which, from time to time, irregularity is a notable feature of the case. Cases in which single extrasystoles at long intervals, or cases in which numerous extrasystoles have been observed only on one or two occasions have been excluded.

have been examined and the mechanism analysed in each case. These cases subdivide themselves as follows :—

| | |
|--|----|
| 1) Complete irregularity of the heart .. | 57 |
| 2) Ventricular extrasystoles | 34 |
| 3) Auricular extrasystoles | 11 |
| 4) Irregularity due to heart-block .. | 3 |
| 5) Gross sinus irregularities | 3 |
| 6) Complex irregularities and paroxysmal tachycardias | 6 |

We see, therefore, that of 114 cases 57 were of the form under consideration, constituting 50 per cent. of the total number. With the exception of groups 4 and 6, the cases were in no way selected. All cases of persistent irregularity which have been observed during the course of my out-patient clinic at the City of London Hospital for Diseases of the Chest, and all cases of the same sort to which my attention has been directed amongst the indoor patients at University College Hospital have been included.

Etiology (based upon 73 cases).

Of the sexes affected, 43 were males and 30 females.

The age limits in this series are 13 to 84. The average age is 41.9 (67 cases).

As regards the remaining etiological features examined, they are included in the accompanying table.

It will be seen that a history of rheumatism* or chorea has been present in 26 cases; in 3 additional cases at least there was a history of one or other in the family alone. Amongst the remainder mitral stenosis was present in 16, pericardial adhesions in one case, and subacute streptococcic endocarditis in one case. Of 64 cases 29 were of undoubted rheumatic predisposition, or had actually suffered from joint affection or chorea. In addition, in 18 instances the rheumatic taint was open to suspicion. The total of 47 cases may be included in a rheumatic group, and for the most part these patients are amongst the youngest of the series. (The average age of 45 cases of the rheumatic group was 34.2; that of 22 cases of the non-rheumatic group 57.7.) 37 cases or 52 per cent. were instances of mitral stenosis, and the relationship to this form of valvulitis is so definite that additional figures relating to it may be given. In dealing specially with mitral stenosis I chose only those cases which came to my out-patient department, for the majority of the cases of mitral stenosis admitted to the

* As a criterion of rheumatism I have taken a past diagnosis of rheumatic fever, or the history of an acute illness with swelling and pain in several joints.

general wards have disordered heart rhythm. Of 72 cases of mitral stenosis collected in this way (in each and all of which curves have been obtained), 57 presented the normal sequence of chamber contraction, and 15 or 20.8 per cent. exhibited complete irregularity of the heart.

DIAGNOSIS.

| | | | | | | | | | |
|--|---------------------------------|-----------------|-----------------------|------------------|-----------------|-----------------------|----------------|-----------|----|
| Rheumatic or choreic history | Mitral stenosis | 21 | .. | .. | .. | .. | .. | .. | 26 |
| | Complete irregularity | 3 | .. | .. | .. | .. | .. | .. | |
| | Pericardial adhesions | .. | .. | .. | .. | 1 | .. | .. | |
| | Granular kidney | .. | .. | .. | 1 | .. | .. | .. | |
| Rheumatism or chorea in family | Mitral stenosis | 1 | .. | .. | .. | .. | .. | .. | 3 |
| | Complete irregularity | 2 | .. | .. | .. | .. | .. | .. | |
| | Mitral stenosis | 10 | .. | .. | .. | .. | .. | .. | 35 |
| | Arterial disease | .. | 6 | .. | .. | .. | .. | .. | |
| | Complete irregularity | 5 | .. | .. | .. | .. | .. | .. | |
| | Granular kidney | .. | .. | 3 | .. | .. | .. | .. | |
| No history of rheumatism or chorea | Aortic disease | .. | .. | .. | .. | .. | 12 | .. | 35 |
| | Aneurism | .. | .. | .. | .. | .. | .. | 2 | |
| | Emphysema and br. | .. | .. | .. | .. | .. | .. | 2 | |
| | Strepto. endocarditis | .. | .. | .. | .. | .. | .. | 1 | |
| | Pericardial adhesions | .. | .. | .. | .. | 1 | .. | .. | |
| | Tuberculous pleurisy | .. | .. | .. | .. | .. | .. | 1 | |
| | Chronic alcoholism | .. | .. | .. | .. | .. | .. | 1 | |
| | Pneumonia | .. | .. | .. | .. | .. | .. | 1 | |
| Not noted | Mitral stenosis | 6 | .. | .. | .. | .. | .. | .. | 9 |
| | Not noted | .. | .. | .. | .. | .. | .. | 3 | |
| | | 38 | 10 | 6 | 4 | 2 | 2 | 11 | 73 |
| | | Mitral stenosis | Complete irregularity | Arterial disease | Granular kidney | Pericardial adhesions | Aortic disease | Remainder | |

The symptoms.

For the purpose of studying the symptomatology of complete irregularity of the heart those patients have been selected in whom the irregularity and its concomitant phenomena were alone present. Dilatation and signs of valvular lesion were absent, and the remaining organs appeared to be normal. Cases in which the affection is paroxysmal are also important from this

point of view, and are included. This selection permits the exclusion of certain symptoms which are not referable to the irregularity itself. It must be acknowledged that the subjective manifestations are few in number, and that they may be almost entirely absent. A certain degree of short-windedness during or after exertion, an occasional fluttering in the neck or chest may be experienced. A general feeling of ill-health, often associated with easy exhaustion, is not uncommon. Gastric discomfort and loss of appetite are not infrequent. The symptoms are more prominent in nervous subjects. Such are the main disturbances in cases in which the ailment is of short standing.

There appears to be a special symptomatology, or, speaking more correctly perhaps, a more profound disturbance at the time of the onset of the irregularity. The actual onset has probably never been recorded, but the symptoms and observations at or about the onset all point to its being as sudden as it is in the case of regular paroxysmal tachycardia. In all, one case of onset in which the arrhythmia became persistent and five cases of the paroxysmal type of complete irregularity have come under my own observation. In the first case the irregularity commenced while the patient lay in bed, and shortly after waking. He was seized with violent palpitation in the chest, a choking feeling in the throat, and inability to "catch his breath." The heart was observed by him to be beating very rapidly and irregularly. The symptoms lasted 15 minutes and were relieved by brandy, but the irregularity is said to have continued until he was next seen; it has been present ever since (*CASE 11*). In three paroxysmal cases (*CASES 2 and 10* and Fig. 9) the change from one type of mechanism to the other occurred without appreciable manifestations* of a subjective nature and usually passed unrecognised. In one of these cases there were physical signs pointing to thoracic aneurism and anginal attacks were frequent, but no relationship could be traced between the anginal attacks and the change of heart action. In a fourth paroxysmal case the first attack was accompanied by great prostration, pallor, fainting, and tonic contraction of the arms and legs (simulating tetany). In the fifth case two attacks occurred. The patient was admitted suffering from streptococcal endocarditis, and post-mortem a large ulcerated area was found in the right auricle. The first attack produced great prostration, exhaustion, and violent palpitation. The second attack, which was similar, proved fatal.

The cases which have come under observation show that the paroxysms may last a few hours or several weeks or months. The symptoms, when present, seem to be more marked at the commencement of the irregularity.

The symptomatology in the majority of patients, cases in which obvious valvular disease or dilatation is present, is that of decompensation in its various degrees. It is not in any way identified with the condition of irregularity itself.

* In one of these the change was from an attack of paroxysmal auricular tachycardia to complete irregularity (Fig. 9).

For further accounts of the symptomatology in this condition reference may be made to the writings of Mackenzie, and to a recent paper by Hewlett²².

The radial pulse curves.

The character of the radial pulse curves in complete irregularity of the heart is so striking that it could not, and as we have seen did not, escape early attention.

Several tracings of the arrhythmia are given by Marey¹¹ (Figs. 199 to 204) as examples of the pulse in mitral insufficiency. The same type of pulse is figured by Fagge⁸ (Fig. 3), Mahomed¹² (Plate IV, Figs. 7, 13 and 16), Walshe¹³ (Plate I, Figs. 8, 10 and 11), Sansom³⁷ (Figs. 112, 122b, 159, 160, 163, etc.), Steell⁶¹ (Figs. 9, 10, 42 to 44, 49, 59, 60, 75, 76, 78 to 82, 86 and 89), and by Broadbent² (Figs. 27 and 36). Numerous figures will be found in Mackenzie's books.

The irregularity is of the most varied description. The pulse may be slow or fast, and the variation in rate is great (30 to 200). The beats may be all of small excursion; more commonly there is a haphazard intermingling of forcible and weak contractions, and the latter are often markedly dicrotic. The radial pulse is often but an indifferent index of the rate of the ventricle; many beats are not transmitted. The pulse rate may be considerably reduced, either as a result of "dropped" beats or as a consequence of the actual slow speed of the ventricle. The beats may show coupling over short or long stretches of curve. The fast types are the commonest, and in these the usual rate of the ventricle is approximately double the normal rate (110 to 150). It is usually at these fast rates that the disorderly character of the pulsation is so prominent. With the slower rates the irregularity is not so prominent, nevertheless, it is always present, a fact which can be determined by careful measurement of the tracings. Where the grade of irregularity is high the condition may be recognised by feeling the pulse; and with experience even the lesser grades of disorder, for example those met with in cases where the pulse is slower, can be identified by similar means, though the method is inevitably uncertain. A Dudgeon tracing is adequate in the majority of patients, and the disorder may be recognised by two criteria. First and most important is the absolute character of the arrhythmia. The heart action is never regular, and seldom or never do two beats of the same character or length succeed each other. In a long curve it is rare to find any two short sections of tracing which have even a superficial resemblance to each other. The pauses betwixt the beats bear no relationship to one another, and in this feature the irregularity stands in marked contrast to all other varieties. The second criterion consists in the absence of a definite and continued relationship between the strength of a beat and the length of the pause which precedes it. A strong beat may follow a short pause, and a weak beat may succeed a long pause. A few examples of the

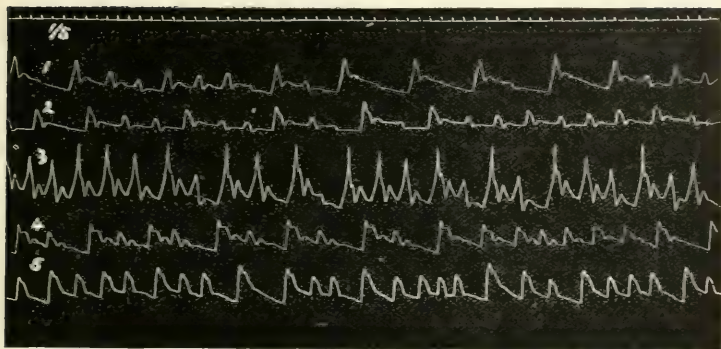


Fig. 1. $\times \frac{5}{16}$ linear. Radial pulse curves taken with a Dudgeon sphygmograph. The time tracing, which applies to all curves beneath it, is in $\frac{1}{4}$ sec. The figure illustrates the general characteristics of the disordered heart action considered in the text.

CURVES 1 AND 2.

CASE 1.—A. H., a man aged 48, admitted to hospital suffering from mitral stenosis of rheumatic origin and general cardiac dilatation. Enlargement of liver, distended veins and dropsy were present. Irregularity complete and persistent; murmurs early and mid-diastolic; venous curves of ventricular form; electrocardiographic curves of usual type (as in Fig. 14 I). The oscillations were maximal when the electrodes were placed over the right auricle.

CURVE 3.

CASE 2.—W. S., a man aged 64, the subject of bronchitis, emphysema and arteriosclerosis. No history of rheumatism. Heart somewhat enlarged to right and left. Heart sounds normal; S. B. P., 150 mm. Hg.* With the exception of shortness of breath on exertion no signs of broken compensation were present. The irregularity disappeared on one occasion for a few days, the pulse regularity was then interrupted by auricular extrasystoles. The *a-c* interval was normal. With the complete irregularity the venous pulse was ventricular in outline, the electrocardiograph was typical, the oscillations were maximal in leads from the parts of the chest wall covering the right auricle. There was no pulse slowing with heavy doses of digitalis.

CURVE 4.

CASE 3.—W. P., a man aged 37, suffering from mitral stenosis of rheumatic origin. Heart enlarged to right and left, dyspnoea and slight liver enlargement, no dropsy. Pulse persistently irregular; ventricular form of venous pulse; electrocardiograms typical; oscillations maximal with electrodes in neighbourhood of right auricle.

CURVE 5.

CASE 4.—R. N., a man aged 65, suffering from aneurismal dilatation of the whole thoracic aorta, pulmonary oedema, associated with arterial sclerosis, emphysema and signs of sclerotic kidney. Dropsy and liver enlargement present. Pulse persistently irregular; ventricular form of venous pulse. Died unexpectedly.

* This blood pressure reading is a measure of the obliteration pressure of the most forcible beats. Blood pressure estimations in cases of complete irregularity are extremely unsatisfactory; the beats force their way through the armlet at widely varying pressures.

pictures presented by Dudgeon tracings are given in the accompanying figure. They may serve with the brief notes attached to them as a guide to the recognition of the type of case with which we are dealing. They illustrate the main points referred to in the text, but the variety shown is so great that they can scarcely be held even as representative of the irregularities which may occur. Numerous and additional examples are scattered throughout the simultaneous tracings which illustrate this paper.

The venous pulse curves.

"The ventricular form of venous pulse" is a term which expresses the only fixed quality manifested by graphic records taken from the jugular veins in these cases. It implies that all prominent and rapid changes of volume in the venous cistern fall within the limits of ventricular systole. The curves corresponding to the individual heart beats vary in their positions relative to each other just as do the radial beats. There may be considerable variation in the amplitude of the separate curves in a given case. This variation is far from instrumental in origin, for close examination reveals the recurrence of a particular type of curve with a given length of pause, a given type of radial beat or a given phase of respiration. As a general rule and in a single case a large venous curve accompanies a large radial curve, but the difference in size from one beat to the next is less in the former than in the latter. A family resemblance between the separate venous beats of a single curve is generally if not always present.

The variation from case to case consists mainly in the relative difference in the height of the several waves and a similar difference in the depths of the depressions which separate them.

The complete curve, corresponding to a single heart cycle, is generally composed of two* or three peaks, and a similar number of dips. The upstroke of the first peak is synchronous with the commencing carotid pulsation at the same level of the neck (though it may precede or succeed it slightly). The downstroke of the last peak starts at a point corresponding to the opening of the tricuspid valves (Mackenzie). It is synchronous with the bottom of the downstroke of the cardiogram, or with a point a little later than the bottom of the dicrotic notch on the carotid tracing. The chief depressions follow the first and last peaks and are very variable in degree from case to case. As a general rule it may be said that the shorter the

* The waves were named by Mackenzie *a* and *v* respectively, and attributed to auricular and ventricular systole; de Vries⁵ has recently shown that they are sometimes met with when the normal heart sequence is present. This accords with my own experience. I do not think that there is any type of the ventricular form of venous pulse which does not find its counterpart in the ventricular portion of the auricular form of venous pulse. It is probable also that with more extended observation the reverse will be found to hold, namely, that, in respect of their systolic elements, duplicates of all forms of the ventricular portion of the auricular form of venous pulse exist in the absence of all signs of the normal auricular contraction.

duration of the abnormal rhythm the deeper is the first as compared to the second depression; and that in old-standing cases the dip in the centre of systole is replaced by a larger and fuller complex of systolic peaks. A definite relationship appears to exist between the mean distension of the veins and the swelling of those veins in systole. Thus, in cases of long duration, in which the veins are more or less markedly dilated, the venous curve is in the form of a prominent systolic plateau. The older conception that the prominence of the venous pulsation is an index of the degree of tricuspid reflux is not without a definite foundation. The curves obtained from patients soon after the onset of the new rhythm and the curves in cases in which compensation is complete generally permit of close comparison with the *ventricular* portions of the venous curves taken from normal subjects (the parts of the normal curves usually marked *c* and *v*). A curve of the kind is shown in Fig. 2 C. In long standing cases, or in instances where compensation is less complete, the first depression (corresponding to the *x* and *x'* dips of the normal curve) is filled (Fig. 2 B and A), and the filling may happen in greater and greater degree until the type assumed is flat-topped and resembles the curve of intra-ventricular pressure (Figs. 2 A and 4 A). The transition from one type to the other may be followed from case to case, or may be seen in one and the same case as cardiac tone and venous filling wax and wane. The flat-topped type also consorts more commonly with rapid heart action, though in marked degree it rarely occurs in the absence of appreciable heart distension. In many curves the smaller and more rapid beats are accompanied by the flat type of curve, and the stronger beats by a bifurcated type (Fig. 2 A). The contrast may be explained by the unequal heart filling under the two conditions. The accompanying figure illustrates several of the types of curve met with, and others will be found in other parts of this paper. It is by no means unusual to see three prominent peaks, concurrent with each heart beat, and such curves bear a close resemblance to the experimental venous curves of Rühl⁵⁵. The relationship of the normal type of curve to the various forms of ventricular venous pulse curve is diagrammatised in Fig. 3. The outlines have been drawn from actual curves, several of which illustrate this paper. The dotted outline is that of the auricular form of venous pulse. The essential difference between this diagram and the somewhat similar ones figured by Mackenzie⁵⁷ and Wenckebach⁵⁸ lies in the fact that it displays transitions between various types of the ventricular form of venous pulse. The original figures were published to illustrate the passage of the auricular form to the ventricular. The view of gradual "paralysis" of the auricle, which they were intended to express, and of the gradual distension of the chamber as a factor in the production of the true ventricular form of venous pulse and its concomitant, irregularity of the heart, has been entirely abandoned. It is perfectly true that dilatation of the auricle occurs, and it is equally true that such distension is accompanied by a transformation of the systolic portions of the venous curve as it has been illustrated. But the distension of the auricle and the deforma-

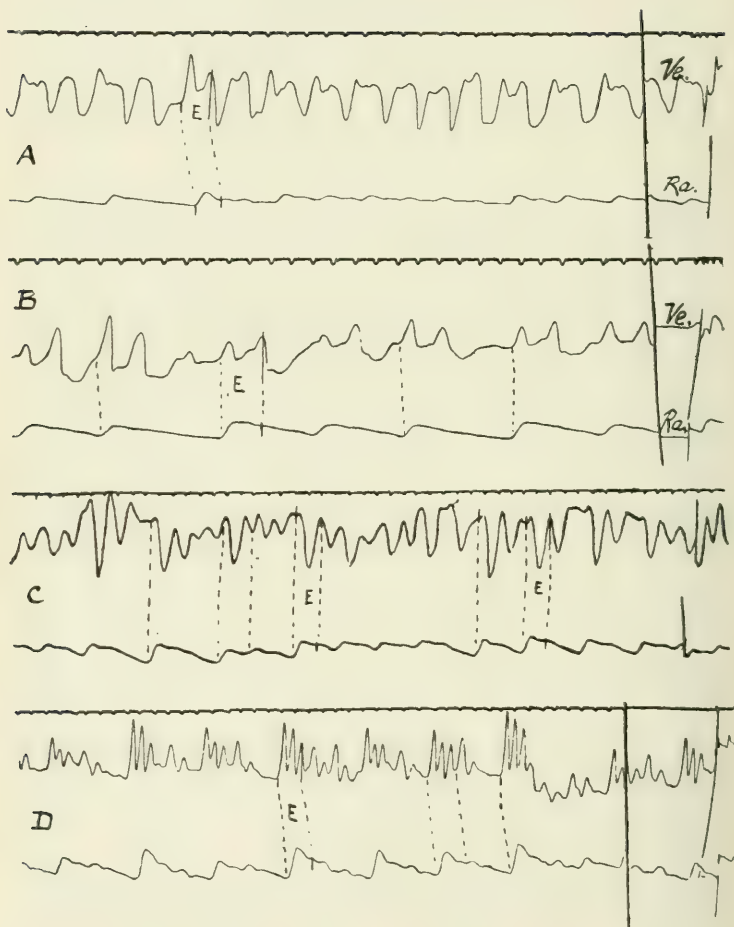


Fig. 2. Simultaneous venous and radial curves from four patients with complete irregularity of the heart and the ventricular form of venous pulse. The figures illustrate some of the different types of venous curve met with in this condition. The venous curves are constant in that all rapid upstrokes lie within the confines of systole (E. E). The dotted lines in this and subsequent curves unite points representing one and the same phase of the cardiac cycle. The heavy vertical lines cutting a whole tracing mark the points where curve has been excised.

CURVE A.

CASE 5.—R., a man aged 39. The mother had rheumatic fever. Admitted for shortness of breath and precordial distress. Heart enlarged right and left, veins prominent and liver dullness increased. No dropsy. Heart sounds weak but otherwise normal. Electrocardiograms typical, oscillations maximal over auricle. Four inches of curve have been excised from this figure.

CURVE B.

CASE 6.—Mrs. K. P., aged 23, the subject of mitral stenosis of rheumatic origin. Admitted with enlarged liver and dropsy. The curves were taken some weeks after admission when the patient had responded well to digitalis. Early and mid-diastolic murmurs; electrocardiograms typical. Eight inches of curve excised.

CURVE C.

CASE 7.—M., a man aged 26, with no symptoms other than slight short-windedness on strenuous exertion. History of rheumatic fever. No cardiac enlargement, no murmurs. Irregularity has been present for two years and has been persistent. The electrocardiograms show prominent oscillations and ventricular extrasystoles. (Fig. 24 is from this case.)

CURVE D.

CASE 8.—Mrs. A., aged 38, suffering from mitral stenosis. On admission dropsy and œdema of lungs were present. Tracing taken several months later, subsequent to digitalis. Compensation had so far improved as to allow her to pursue her ordinary duties as housewife. Heart enlarged to right and left; early and mid diastolic murmurs. Veins not prominent. Irregularity persistent. Two inches of curve excised.

tion of the venous curve may take place, while, during the transition, the presystolic auricular contraction is present, or while, during the transition, the co-ordinate systoles of the auricle are suspended. As we shall see at a later stage the ventricular form of venous pulse may be conspicuous even in its plateau form, while the normal heart sequence is maintained (*CASE 14*), and, as we have already seen, the usual or normal systolic portion of the venous pulse may be found (the type with the deep x and x' depressions) and yet the signs of co-ordinate and presystolic auricular contraction may be entirely in abeyance. It should be clearly comprehended that two

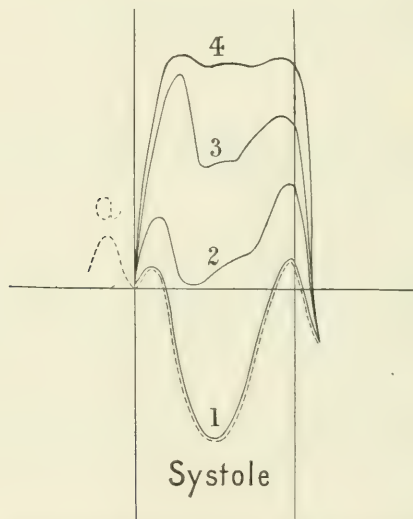


Fig. 3. A diagram illustrating the relationship of the auricular and ventricular forms of venous pulse, and the more common variations in shape to which they are liable. The dotted line represents the usual or physiologic type of the auricular form of venous pulse. The continuous lines represent the ventricular portions of types of curve met with in auricular and ventricular forms of venous pulse.

perfectly distinct phenomena exist, a sudden disappearance of all signs of the normal auricular systole, and a gradual increase of pressure in the right side of the heart. The lack of due appreciation of this essential distinction has led in the past to many misconceptions of the conditions with which we are dealing, and to the faulty interpretation of many curves. The diagram may stand as an example of the transition of the systolic portion of either

auricular or ventricular form of venous pulse curve, from the compensated to the decompensated type, or from the type with perfect to the type with imperfect venous flow. In brief, it may be said that there is but one distinctive quality between auricular and ventricular forms of venous pulse, and it consists in the absence of the auriculo-systolic or *a* wave from the former. Individual cycles of a curve, which is an example of the ventricular form of venous pulse, can be identified as such with certainty only by attention to this fact.

These considerations bring us to a subject of importance to those for whom the application of graphic methods is difficult or impracticable. The question may be asked—Can the ventricular form of venous pulse be recognised with the unaided senses? The reply to this question is that it can be recognised in a very large number, in fact, the majority of cases, if note is taken of the conjoined phenomena. The first essential in its recognition is the finding of an irregular pulse. If the heart is beating arrhythmically the ventricular venous pulse may be identified in almost all cases in which it is prominent. Each beat of the heart as felt at the apex is accompanied by a pulsation in the veins of the neck, which starts with the systole and preserves this relationship from beat to beat. Now the prominence of venous pulsation is very variable. It may be so marked that at each systole the girth of the neck is increased by an inch or more. The pulsation commonly attains the angle of the jaw, and not infrequently it displaces the lobe of the ear. In one case I have seen it extending as far as the summit of the scalp and have recorded it above the zygoma. But a type so marked is exceptional. Much oftener the pulsation is confined to the neck. If, under these circumstances, the superficial veins are conspicuous, it is readily recognised. But in cases where this is not the case I have seen it mistaken for arterial pulsation on several occasions. The error may be avoided if it is borne in mind that the pulsation is a volume change and not a pressure wave; it is often visible, but the fingers rarely appreciate it. "Diastolic collapse" often accompanies it, and is merely a descriptive term for the impression left on the sight by the rapid volume decrease which occurs at the end of systole. This volume decrease is shown in the curves, and has been referred to previously. In early and compensated cases the pulsation is rarely recognised by the ordinary means, for usually in such instances the visible pulsation is complex; resort must then be had to the graphic method. A venous tracing may often be secured where no venous pulsation can be seen.

Certain waves which occur in diastole.

It has been stated that the ventricular form of venous pulse is composed of waves of which the prominent and rapid ones fall during systole. It is also true that waves occur within the limits of diastole. The earlier interpretations of the curves in which they are found are, almost without exception,

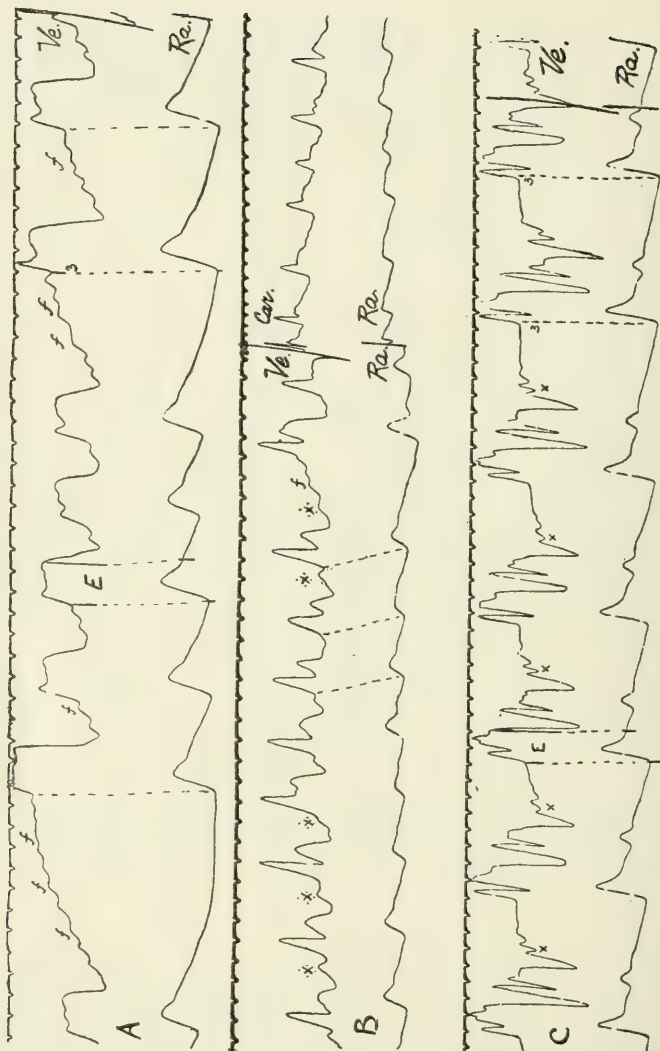


Fig. 4. Simultaneous venous and arterial tracings from three patients with complete irregularity of the heart. Illustrating the several types of wave which occur in diastole when the venous pulse is ventricular in form.

CURVE A.

From a patient whose case is described later (*CASE 12*). The curve shows fibrillation waves, *fff*, during the long diastolic pauses. These are superimposed upon long stasis waves. The systolic portion of the venous curve is of the plateau form.

CURVE B.

Taken from *CASE 5*, but at a later date, when cardiac tone was partially restored. There is a wave in diastole marked * which is ascribed to closure of the tricuspid valves at the end of filling. In the longest pause small oscillations, *f*, appear.

CURVE C.

CASE 9.—From a man, aged 49, suffering from mitral stenosis of rheumatic origin. The heart considerably enlarged to right and left. Dropsy and pulsatile liver. Early diastolic murmur at apex. The pulse is completely irregular, except that each large beat is followed by a smaller one at an almost constant interval. In the diastolic portion of the curve a gradual rise ends in a plateau, and where the two meet three small oscillations occur (marked *x*). They were accompanied by a valvular sound at the apex and in the neck. They may be attributed to closure of the tricuspid valves.

erroneous. The waves in question have been attributed repeatedly to co-ordinate contraction of an irregularly beating auricle (in a recent paper Magnus-Alsleben has fallen into similar error)⁴².

The view has been expressed that apart from the auriculo-systolic wave there is no essential distinction between the individual venous curves in the normal and abnormal conditions*. It will be necessary at a slightly later stage to note a single exception to this rule. But, for the time being, we may enquire whether any waves occur in the diastolic reaches of the normal venous pulse, apart from those allotted to auricular systole. There are waves of two kinds, and precisely similar waves are found during diastole in the condition which we are considering. There is a wave which has been termed by Morrow¹⁶ the "second onflow wave," and its causation is assigned to the overflow into the veins when in a long diastole the heart is already full, or to the increase of pressure in the ventricle during the filling. It is seen to advantage in the accompanying figure (Fig. 4). At the commencement of tracing A there is a long pause, and during the whole of it the veins are steadily swelling. It is also prominent in tracing C and is shown to a lesser extent in tracing B. The fixed relationship of this stasis wave to the preceding systole and the variation of its extent with the length of diastole permit its recognition.†

The second type of wave was first described in the normal condition by Hirschfelder²³, and has been attributed to the closure of the tricuspid valves at the end of ventricular filling (Gibson¹¹). But there is evident misconception as to the extent to which this interpretation can be applied. The snapping to of the auriculo-ventricular valves will not serve in explanation of a permanent increase in venous volume. The type of wave produced must be carefully distinguished from that produced by stasis. If the wave is followed by a dip it may perhaps be assigned to a valve movement, but only, I think, such part of the wave as is definitely raised above, or depressed below, the general sweep of the stasis wave itself. Waves belonging to this class are seen in Fig. 4 B and C. In tracing C, and just at the summit of the main sweep of the stasis wave a triple vibration (marked ×) with constant time relationship to the preceding systole is plainly visible. It was accompanied by a distant valvular sound at the apex and base of the heart (cp. Gibson¹¹ on third heart sound), and by a distinct double clicking sound in the veins of the neck. In tracing B we have an example in which the portions of the diastolic waves attributable to stasis and valve movement are more difficult to unravel. The longest diastole, just antecedent to the stops, is of value in this connection. In this diastole we see the general sweep of the stasis wave and superimposed upon the first part of it is the wave marked ×. The same wave is found in earlier portions of the same

* The statement is not affected by the fact that one type of ventricular curve is more common in the normal and another type in the abnormal condition.

† Its inclination to the vertical is a rough index of the rate of venous flow.

curve, and the comparison with the later diastole allows us to gauge the extent to which stasis aids in its production in these earlier diastoles.

We may now turn to another type of diastolic wave, the most important of all. It forms the exception to the remarks previously made as to the resemblance between the ventricular and auricular types of venous curve. These undulations are only met with as an accompaniment of the ventricular form of venous pulse. They are seen but occasionally, and only when the pulse is slow (Wenckebach⁶⁶). They are well marked in tracing A, and are more obscurely figured in tracing B (marked *f*). They are also shown in the photographic curve (Fig. 19). They are multiple, and the rate may be from 350 to 500 per minute. Their irregularity renders it difficult to estimate the rate other than approximately. They were first described by Wenckebach⁶⁶ in 1907; in discussing Cushman and Edmund's paper on auricular fibrillation and the relationship of the latter to complete irregularity, he stated that in the clinical condition he had seen small venous waves which might be attributed to small contractions in the auricular walls. Later, in the same year, they were figured by Mackenzie⁷, who also suggested that they might arise as a result of auricular fibrillation. The relationship of this fibrillation to the view adopted in his papers, namely, the nodal origin of the rhythm, is not explained, and in a later publication⁶⁷ (p. 299) the idea was abandoned. ("From this observation, I now recognise that what I had taken for waves due to fibrillation of the auricle were really due to a fault in the method of registration, wherein by compressing the vein with the receiver I had artificially produced thrills which appeared as waves in the tracing.") Certain observations, which will be discussed more fully at a later stage, point to the conclusion that the oscillations are in reality the outcome of fibrillary movements in the auricle. At the present time it will be sufficient if I state that the thrills in question have not come under my personal observation, that I am inclined to attribute the thrill in this instance to the oscillations rather than the undulations to the thrill, and that in chlorotic cases where the auricular type of curve is obtained to perfection such vibrations are absent.

The electrocardiographic curves obtained by leads from the right arm and left leg.

Electrocardiographic curves from cases of complete irregularity of the heart have been published by Einthoven⁶⁸ (Figs. 17 and 31), and later by Kraus and Nicolai⁶⁹ (Fig. 14), Hering⁷⁰, and Rothberger and Winterberg⁷¹.

The following account is based upon curves taken from thirty cases.

Firstly, the curves consist of tall peaks R, corresponding to the commencement of ventricular systole, and scattered throughout in irregular profusion. Their arrangement is obviously due to the arrhythmic action of the ventricle (cp. Fig. 15 and its accompanying radial curve). The direction of the electric variation, of which the peak R is an expression, indicates

negativity of the arm electrode, or primary activity of the base of the heart. The variation is the same as that which occurs in the normal subject and is an evidence, as Hering has pointed out, that in this condition the ventricular contraction commences at its normal starting point. The remainder of the curve and its comparison with the normal (normal curves are shown in Figs. 12 and 16) justifies this conclusion, as we shall see in the sequel. I have long suspected that the peaks R in the abnormal curves are relatively higher than in the normal curves. For curves of good excursion are always obtained with facility even while the instrument is adjusted at a comparatively insensitive point and in patients with high resistances. The comparison may be made in Figs. 15 and 16, taken from the same patient within two days of each other; it may also be made in Fig. 9 (it is mentioned in the explanatory remarks attached to the figure*).

A comparison of the height of the peaks R with the strength of corresponding radial beats in synchronous tracings reveals the fact that there is no fixed proportion between them (Fig. 15). A very similar, if not identical, phenomenon is present in the condition known as heart alternans (for the experimental fact, see Hering¹⁰; the clinical parallel has been observed more recently (*CASE 15*)).

Apart from the peaks R the normal ventricular curve consists of slight depressions following them, and these in turn are succeeded by broad waves designated T. The T variations are also seen in curves from cases of complete irregularity. They are often very obscure, and this obscurity is the result of the presence of certain special oscillations upon the curves. The variation T is plainly perceptible in Figs. 13 I, 18 I and 19, while it is overshadowed in Figs. 14 I, 15 and 23. At times it is quite as prominent and almost as regular from cycle to cycle as in the normal curves (Fig. 19). The occurrence of T is of importance because it demonstrates, what would otherwise be uncertain, that the ventricular contraction starting at the base pursues its usual path in the ventricle†.

The most striking feature of the electric curves is the absence of all sign of the regular presystolic variation, which accompanies all normal heart beats (P in Fig. 16), and the presence of that which replaces it, namely a number of irregular oscillations varying in form and prominence. In leads from arm and leg these oscillations are often marked in amplitude, and the latter may equal if it does not exceed that of the usual auricular variation P (Fig. 23). In other curves they may be far less conspicuous, and may be

* An increase in the size of the peak R as compared with the normal was also seen in the cases of regular paroxysmal tachycardia which have already been placed on record^{20 & 22}. It would appear that both in complete irregularity and in the regular paroxysms the heart, as a whole, is in a state of hyperirritability. The curves seem to indicate at all events that in such cases the energy developed and used up is great in proportion to the work accomplished. In other words, the heart is working at a disadvantage. Einthoven⁶ found no increase, but in one case a decrease, in the size of R with an increase of rate following exercise (Figs. 26 to 29 of his paper).

† The variation T is attributed by Gotch^{12 & 13} to a return of the contraction to the base of the heart (activity is represented electrically by negativity).

distinguishable only from place to place (Fig. 24, *f f*). In one form or another they have been invariably present in all the cases examined. They are a constant feature of cases of complete irregularity of the heart and occur in no other condition. They are responsible for the distortion or concealment of T in the arm-leg leads; the clean cut character of R is never affected, and this is due to the quickness of the movement. The oscillations appear in a purer form when certain special leads are adopted, but the curves obtained in this way will be more appropriately dealt with in a subsequent section.

The oscillations are most conspicuous when the pulse is slow or during a diastole of unusual length. For during systole they fall upon the ventricular elements of the curve and their definition is obscured. When the heart beat is rapid the individual waves may be difficult to separate, but their presence is known from the fact that the T waves vary greatly in form or are entirely overshadowed (Fig. 15), and by the appearance here and there of single undulations on the curve which can only be ascribed to the same cause. The deformity of the curve as a whole, produced in this manner, is so characteristic of the condition that, once recognised, the curves are never mistaken for those obtained in any other affection.

COMPLETE IRREGULARITY OF THE HEART IS THE RESULT OF AURICULAR FIBRILLATION.

The irregular oscillations seen upon galvanometric curves are due to an inco-ordinate contraction of some portion of the heart; they are not a direct result of structural change in the heart, and are independent of movements of the somatic musculature.

It might be suggested that the oscillations in question are dependent upon structural changes in the heart muscle, and that the propagation of the contraction wave, along the path usually taken, is hindered or modified by the presence of areas of tissue affected by disease. But we are in a position to deny that the oscillations are attributable to this cause.

Such a hypothesis is at once weakened when it is known that the oscillations bear no relationship in their extent or frequency to the objective signs of damage in the myocardium. For while a patient may be suffering from obvious and gross myocardial change, yet if the sinus rhythm is dominant the oscillations are absent; and, on the other hand, patients showing no signs of gross myocardial affection, patients in whom there is no dilatation and in whom there is little disturbance of the circulation even after strenuous exercise exhibit fully developed oscillations, provided that the pulse is completely irregular. If further evidence is required it will be

found in two cases in which a comparison of the normal and abnormal mechanisms in the same subject was secured*.

CASE 10.—G. P., aged 77, was admitted under the care of Dr. Mackenzie, to whom I am indebted for opportunities of examining him, in September, 1909. There was no history of past illness, and rheumatism and chorea were unknown in the family. He complained of slight cough and expectoration, and huskiness of voice of four months' duration. Anginal symptoms had been present. There had been no shortness of breath, palpitation, giddiness or dysphagia.

Condition, 22.10.09.—A strongly built man; the face weather beaten. The voice is husky, laryngeal examination shows abductor paralysis. A slight grade of cyanosis is present. The arteries are thickened, the pulse is completely irregular; the venous pulse is of the ventricular form. The heart's apex is obscured by emphysema. The right line of dullness is $\frac{1}{2}$ inch and the left $3\frac{1}{2}$ inches from the middle line. There is an area of dullness extending into the second left space and at this point systolic pulsation was present upon admission. But for the irregularity the heart sounds are normal. The urine is normal.

The case may be summed up as probably one of aneurism of the thoracic aorta, associated with angina and complete irregularity of the heart. Subsequent to his admission he has had many anginal attacks, some of a severe grade. There have been times when the pulse is slow, and on such occasions it is regular and the venous pulse has been of the auricular form, and times when it is fast and irregular, the venous pulse being then ventricular in outline. The paroxysms of irregularity have been numerous, and they have generally lasted for 24 hours or more. On several occasions the pulse has been irregular for several days together. On the other hand attacks of comparatively short duration have occurred. There have been no definite symptoms at the onset or offset of attacks, and the patient has been unaware of the abnormal cardiac mechanism when it has been present. The anginal attacks have had no relation to the periods of irregularity.

Two of the curves (Figs. 15 and 16) obtained from this patient were taken within 48 hours of each other. Upon the day when the first electrocardiogram was obtained polygraph curves showed the presence of complete irregularity and the ventricular form of venous pulse. The electric curve corresponding (Fig. 15) is of the form which we have been considering. The peaks R are separated by stretches of curve of an irregular character. No two pieces are alike, and the T variations are obscured by the oscillations which are present. Two days later the pulse was regular and the jugular curve demonstrated a prominent *a* wave. The corresponding electrocardiogram is given in Fig. 16. In it the disappearance of the oscillations is associated with the return of the auricular variation P, while the remainder of the ventricular curve is of a perfectly normal type. Curves showing the normal rhythm within half an hour of the cessation of an attack have since been obtained from this patient. They were of a perfectly normal type. Digitalis, given in doses sufficient to produce toxic effects, had no retarding influence during the periods of irregular tachycardia.

* A third case will be found in a later section and the curves are illustrated by Fig. 9.

CASE 11.—A. G., a barman, aged 24, was admitted to the out-patient department at the City of London Hospital on 8-12-09, complaining of cough with blood-stained sputum, and pain in the left shoulder. These symptoms had been experienced for some months; but he has had earlier attacks and is known to have suffered from heart disease for several years. He has never had rheumatic fever or chorea and there is no history of either in the family. He has never had dropsy.

Condition, 8-12-09.—The right limit of cardiac dullness is 2 inches, and the left 5 inches, from the middle line. There is a marked presystolic thrill at the apex; a rough crescendo murmur leads up to an accentuated first sound. The second pulmonary and aortic sounds are normal. There are no signs of liver enlargement or dropsy, but there are scattered rhonchi over both lungs. Auricular extrasystoles are frequent and interrupt an otherwise regular heart rhythm. Each extrasystole is accompanied by a first and usually by a second sound, and a dull valvular sound precedes the first sound, but there is no murmur. The *a-c* interval is increased. A polygraph curve is shown in Fig. 5a and electrocardiograms in Fig. 12. 13-12-09. —On this day the patient's condition was identical with that already described. He was placed on tincture of digitalis *mX* t.d.s. 18-12-09. —The patient awoke in the early morning (he has remained in bed since he first attended) feeling ill. He experienced violent palpitation accompanied by a choking sensation in the throat and difficulty in breathing. He states that his heart was beating rapidly and irregularly. Brandy gave him relief but the irregular action of the heart remained. The attack lasted $\frac{1}{2}$ hour. He has never had palpitation before which in any way resembled it. 20-12-09. —On examination the right limit of cardiac dullness is $1\frac{1}{2}$ inches and the left $4\frac{1}{2}$ inches from the middle line. The heart is absolutely irregular, and the venous pulse is of the ventricular form. The auriculo-systolic murmur is no longer present, but is replaced by a murmur of very similar quality which occupies early diastole and continues into the mid-diastole of the longer cycles. The murmur consequently fills the diastole of the shorter cycles. The polygraph curve is shown in Fig. 5b and electrocardiographic curves in Fig. 13. The digitalis was omitted on 20-12-09, but was readministered in larger doses at a later date. The pulse subsequently slowed down in the characteristic fashion, dropping at times to 40 and 45. The digitalis was then relinquished, and the pulse rate returned to 90-120.

Briefly, the case is one of old standing mitral stenosis coming to hospital for an attack of hæmoptysis. Within ten days of attending (and possibly as a result of the digitalis) a normal rhythm interrupted by auricular extrasystoles gave place to complete irregularity of the heart. This irregularity has been present ever since.

Fig. 5a is a polygraph curve taken from this patient on 8-12-09. It shows the normal sequence of chamber contraction, but the *a-c* interval is increased to 0.28 sec.. The rhythm is interrupted by frequent auricular extrasystoles (the premature auricular waves are marked *a'* in the curve) of which three examples are shown. The electrocardiographic curves taken upon the same day are exemplified by Fig. 12. The upper curve of this figure consists of parts of four normal contractions and of two auricular extrasystoles. Reading from left to right, we see a normal beat, accompanied by P, R and T variations; this is succeeded by a second beat of the same character except that the T variation has a premature P wave superimposed upon it; its height is consequently exaggerated. The premature P variation is followed by the R and T peaks of the premature ventricular systole, and the latter is followed by a pause which is not fully compensatory. A normal contraction, an auricular extrasystole and a portion of a normal contraction complete the curve. In the lower curve similar events are shown. Here three contractions are followed by a pair of extrasystolic beats arising

in the auricle, and the curve ends with a normal contraction following a short pause. The features of these curves to which attention is directed are several. The P-R intervals of the normal beats is increased, amounting to a full 0.2 sec.. The P-R interval of the extrasystoles is difficult to measure, but certainly exceeds this fraction. The curve is clean cut and shows no trace of oscillation.

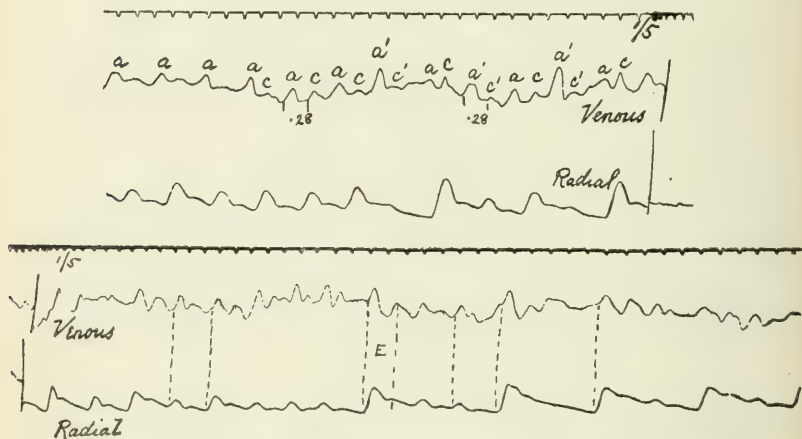


Fig. 5 *a* and *b*. Two polygraph curves obtained from CASE 11, on 8-12-09 and 20-12-09 respectively. Tracing *a* shows a venous curve of the auricular form, and auricular extrasystoles are present. The *a-c* intervals are increased. Tracing *b* shows a curve of the ventricular type, the pulse is completely irregular.

Fig. 5*b* illustrates the condition present two days after the onset of the complete irregularity and twelve days later than the occasion on which the preceding tracings were secured. The polygraph curve shows complete irregularity of the arterial pulse, and the ventricular form of venous pulse. The electrocardiogram, taken on the same day, is given in Fig. 13 *I* (Fig. 13 *II-V* will be discussed later). The curve is characteristic of the condition, and is composed of peaks R, the remains of peaks T, and numerous irregular oscillations. There is no sign of the normal P variation. The dilatation of the heart had distinctly diminished, and the general condition had improved, at the time when the second group of curves were taken.

Now as it is impossible to allow either in the first case or in the second that there was any material difference in the condition of the heart muscle during the brief intervals which intervened between the occurrence of the

normal and abnormal types of curve, for in both patients the cardiac affection was essentially a chronic one, so it is equally impossible to agree that the oscillations displayed were directly dependent upon myocardial change. On the other hand the cases provide very suggestive evidence that we are dealing with a temporary inco-ordinate action of a limited portion of the heart muscle; and as the evidence of normal activity in the auricle is absent it is essentially towards that chamber that our attention should direct itself. The cases demonstrate conclusively the interdependence of the abnormal type of heart curve and the gross irregularity. Further, they afford a strong argument against the view adopted by Hering¹ that the oscillations have their origin in the somatic musculature. The normal and abnormal curves were obtained under precisely similar conditions.

It is perfectly true that many electrocardiograms show traces of variations produced by contraction of the muscles of the body wall or limbs, and at times it may be difficult to exclude this complication from the curves. But the oscillations of which we are speaking bear no relationship to the extent of such movements. Muscular movements give rise to irregularities in the curves when a patient trembles or fidgets. In the great majority of such cases these extraneous vibrations can be identified at once by their general appearance and rate. If precautions are taken in the avoidance of elderly or tremulous subjects, if the recumbent posture is adopted, and if in a warm room absolute stillness is enjoined and enforced, no such irregularities appear in subjects in which the heart sequence is normal. Oscillations are invariably present in the class of patient considered, whatever the precautions employed. They are of much the same degree from day to day and from hour to hour in the same subject. They are equally prominent when leads from the two arms are adopted, but vanish almost completely if the electrodes are attached to the two inferior extremities. The proposition, that they are part and parcel of the heart beat as it is represented to us electrocardiographically, is unequivocal. Very numerous and special leads have been devised and employed for the exclusion of their origin in abdomen, limbs and head and neck. The special leads show that it is a matter of indifference, so far as the amplitude of the oscillations is concerned, as to how great is the extent of somatic musculature which lies beneath and between the electrodes. They demonstrate that the excursion is controlled by the proximity of the heart to the leads.

The special leads take us a step further, for they make it clear that it depends upon the part of the heart approached as to how conspicuously the oscillations will appear.

The irregular oscillations arise in the vicinity of the auricle; the ventricular electric complex in complete irregularity is of the normal form.

Special electrodes were employed, composed of small circular copper plates, and these were fixed to the chest wall by means of a layer of stiff

flour paste made up with a large addition of common salt. A great variety of curves can be obtained in the normal subject by the adoption of the many leads which offer themselves, but with these we are not at present concerned; our attention may be confined for the time being to the amplitude of the oscillations which occur in patients who manifest complete irregularity of the heart. The oscillations are never seen and no vibrations are found, which in any way resemble them, in normal subjects or in patients who exhibit the normal sequential cardiac mechanism. But in cases where the pulse is irregular and the ventricular form of venous pulse is present they are invariable. The analysis, which the chest leads afford, is provided most strikingly by patients in whom the right auricle is enlarged, for in these a larger area of the auricular wall is in apposition to the chest wall; but the phenomena which are here described are not limited to such cases, though present in them in greater degree.

Fig. 13 shows five separate leads. *I* is from the right arm and left leg, and has been mentioned already. The remainder, *II-V*, are from the chest wall and were taken at the same time and under similar general conditions. *II* is the curve yielded by electrodes, one (the arm electrode) placed upon the sternum at the level of junction of the second rib, the other (or leg electrode) upon the apex. The ventricular complex is represented by a curve similar to that often obtained in arm and leg leads from normal subjects; oscillations are also seen on the curve, but they are not prominent except towards its termination. *III* was obtained by moving the apex electrode to the fourth space on the right side and one inch from the sternal margin. The ventricular peaks are comparatively small, and the oscillations are maximal. The leg electrode was next replaced at the apex and the arm electrode was fixed, first in the third space in the anterior axillary line on the left side (*IV*) and later, just below the costal margin three inches internal to the apex beat (*V*). The curves may be taken as representing in the main the pictures yielded by left and right ventricles respectively. They are almost entirely free of oscillations, and show regular and clean cut variations in the latter part of each systole.

The separate leads which we have examined, and numerous leads from other parts of the chest wall, demonstrate at the outset that the oscillations are conspicuous or the reverse according to the proximity or otherwise of electrodes and right or superficial auricle. The conclusion is obvious and beyond question. Of the area of heart superficies which is in relationship to the front of the chest wall it is only over that portion of it which may be termed auricular that the maximal oscillations are produced, and as the heart is admitted as the source of the oscillations their origin may be traced to the auricular portion of it.

Separate leads from the chest wall have been obtained in a large number of patients with the irregularity in question, and they all yield similar results. Two further examples are given in Figs. 14 and 18. The explanations of the figures may be consulted for the details of the leads.

The special curves give an analysis of those obtained by means of the usual arm-leg leads, and show that the latter are constructed by the superimposition of current curves of auricle and ventricle. They explain the deformation of the variation T and show that the variability of this peak from cycle to cycle is the result of the combination of the currents derived from the two sources, and that it is not an anomaly of the ventricular complex itself.

Those curves which are obtained by means of leads from the area overlying the auricle give the purest pictures of the oscillations which may be gained in the human subject (it is possible that œsophageal leads would give still more distinctive tracings) and allow a more detailed study of the oscillations.* Obtained in this way they are found to vary in rate between 400 to 600 per minute, but the usual rate approaches 500 very closely. They frequently have a character, which, though at present inexplicable, is remarkable, and it is seen to advantage in Fig. 13, *III*. The individual oscillations rise abruptly and fall away more gradually. It is a trait not infrequently manifested by the undulations found with arm and leg leads, but in these it is seldom so clearly defined.

Certain deductions from the clinical findings.

The outstanding feature of the records from cases of complete irregularity of the heart is the entire absence of all sign of the normal auricular systole. It has been shown time and again that, while in normal subjects and in patients suffering from all other forms of heart irregularity or cardiac disability the auricular systole leaves a definite impress either upon the cardiogram, upon the venous volume curve, upon the œsophageal curve (Minkowski⁴⁵, Rautenberg⁴¹, Young and Hewlett⁴⁶ and other writers), or upon the electrocardiographic curve, such evidences of its normal activity are consistently wanting by each and all of the graphic methods in the group of cases which is engaging our special attention⁵².

The conclusion which it is impossible to avoid, a conclusion which is accepted by all those who have given reasonable attention to the subject, is that the normal presystolic auricular contraction is in abeyance, temporarily or permanently.

Paralysis of the auricle has been suggested, but little support is now found for this hypothesis. The conditions of the circulation are often such that it is impossible to suppose that the pressure in the auricles is increased. Moreover it is dubious whether we are justified in applying the term paralysis to heart muscle, if we mean by paralysis complete inactivity of the muscle. The maintenance of a state of complete flaccidity in cardiac muscle, surrounded by conditions favourable to its nourishment and to its contraction,

* Very large oscillations may be obtained by placing one electrode over the right auricle in front and the other in the neighbourhood of the angle of the right scapula.

for an appreciable length of time, is a proposition foreign to the experience of experimentalists. A deprivation of its functional powers would lead us to expect, from the analogies provided by pathology, an obliteration of its macroscopic and microscopic characteristics. The observation of hypertrophy in the auricle at autopsy, led Mackenzie to abandon his earlier view of paralysis and influenced him in concluding that the auricle is active. The view was supported by the reappearance of signs of auricular contraction in paroxysmal cases. We are led to a precisely similar contention by the evidence yielded by the electrocardiographic curves. The auricle is the seat of an electric disturbance of a peculiar yet distinctive nature. The constancy of the oscillations, their unique appearance and *their presence throughout the whole of the cardiac cycle*, is responsible for the convictions that they are an essential feature of complete irregularity and that *the activity of the auricle is continual*.

Co-ordinate contraction of the auricle at any period of the cardiac cycle other than that of ventricular systole can be readily excluded. Co-ordinate and simultaneous contraction of auricle and ventricle can also be set aside, for, as will be stated in the sequel, it gives rise to an entirely different clinical picture (see p. 360).

As a whole, the evidence points in the most convincing manner to the conclusion that co-ordinate contraction of the auricle is absent, and to the conclusions that activity is present, and that this activity is a continuous one.

In experimental work we encounter but one variety of auricular activity in which inco-ordination of the separate fibres is present, and this mechanism is one in which the auricle is in unceasing movement. It is the state known as fibrillation or delirium.

The remainder of this communication, therefore, in so far as it deals with the mechanism of the irregularity, will be directed in the main to a comparison, of as searching a nature as possible, between complete irregularity in man and auricular fibrillation as it is induced in the lower animals. For it is upon this comparison that the survival or overthrow of the hypothesis suggested, namely the identity of the two conditions, must ultimately depend.

Oscillations similar to those characterising complete irregularity of the heart in man are found experimentally when the auricle is fibrillating, and these oscillations are produced in the auricle as a result of the fibrillation.

For the purpose of experiment dogs have been employed. They have been rendered insensitive with morphia and paraldehyde, and during the course of the experiments complete or deep surgical anaesthesia has been maintained by the administration of a sufficiency of ether. Fibrillation of the auricle has been induced by faradic stimulation of an auricular appendix. The auricle was exposed by one of two operative measures, by making a

window in the chest wall, or by splitting the sternum and exposing the whole heart. Utilising the former route a small incision has been made in the pericardium and two fine insulated wires being attached to the auricle, the opening in pericardium and chest wall has been closed. By withdrawing the air from the chest the natural conformity of the chest and spontaneous respiration could be restored. The second method has been confined to experiments in which it was necessary to obtain synchronous myocardiograms from auricle and ventricle or to those in which electrocardiograms taken by means of direct leads from the heart were desired. Simultaneous arterial curves were obtained with Hürthle's manometer, simultaneous venous curves by employing portions of the polygraphic apparatus.

The electrodes adopted for the galvanometric leads were of two kinds. In leading from the right fore-paw and left hind-paw the clinical electrodes were utilised. In leading direct from the heart the flexible electrodes described by Gotch* were found to be most serviceable. The auricle was faradised until fibrillation was established, the stimulation was withdrawn and the curves taken before, during or after the return of the normal or sequential contraction.

The oscillations which are obtained experimentally as a result of faradic stimulation of the auricles are unique, for they occur in no other experimental condition. They are seen in Figs. 20 and 22. They consist of variations which succeed each other rapidly, at a rate, in the experience of these experiments, varying approximately from 500 to 900 per minute.* They replace the usual P variations of the normal rhythm and produce the same deformation of the T variations as in the clinical curves. In leading from the terminations of superior and inferior vena cava, the oscillation is sometimes characterised, as is the clinical oscillation, by its more abrupt rise and more gradual fall (Fig. 31 II).

Though never absolutely regular, yet at times the spacing is remarkable for its tendency to regularity, a quality noted in the clinical curves. They continue throughout the whole of the cardiac cycle.

The proposition that these variations are generated in the auricle and that they depend upon the delirium in the walls of that chamber is easily substantiated. They are only present when the auricle fibrillates, and are entirely absent from the curves yielded by the same animals when the normal rhythm is re-established. Figs. 20 and 21 are two simultaneous electrocardiograms taken from a single animal within a few minutes of each other. The first, during an auricular fibrillation period, exhibits the oscillations; the second, after the re-establishment of the normal sequence, shows none, but the P variations have reappeared.

There is a relationship between the rate and amplitude of the electric oscillations, and the vibrations seen in myocardiograph curves. It is well

* The estimation of the rate of oscillations is necessarily only approximate, for they are irregular. The rates were calculated where several similar oscillations succeeded each other and the finest vibrations have been neglected.

known that auricular fibrillation may be of many grades, the movement of muscle levers is fine or coarse in the same experiment or from animal to animal. It is only rarely that an actual correspondence can be found between the individual muscle movements and the electric variations, and this is to be expected, for the whole auricle is active, and only a small portion of the muscular movement is recorded. Nevertheless, correspondence may be found in some degree. When the muscular movement is small, and the vibration of the lever rapid, the oscillations tend to be of small excursion and, as seen under vagal stimulation, may reach a rate of 900 or more per minute.* With the coarse fibrillary movements on the other hand, the electrical variations are of greater amplitude and are slower. Fig. 29 shows simultaneous curves from ventricle and auricle, and an electrocardiogram. In the left hand portion of the figure the auricle is fibrillating, the ventricular beats are irregular, the movement in the auricle is of the coarse variety. In this instance the auricular muscle, though fibrillating, appears throughout to be on the borderland of a return to co-ordinate contraction. Thus in the last half of the fibrillary period the separate vibrations, as seen in the muscle curve, are almost though not absolutely regular at a rate of 450 per minute. The movement in the first half of the fibrillary period is more disorderly and a little more rapid. The figure is a reduction of a greatly magnified photograph of the original curve. During the whole of the fibrillary period it is possible to establish a definite relationship between the individual movements expressed by the auricular curve and the oscillations which appear upon the electric curve. During the last half of the fibrillary period (R' to R^{12}) an oscillation falls with each of the peaks R and with each of the variations T . As a result the height of these waves is enhanced, and a picture bearing a superficial resemblance to 2:1 heart-block is produced. The rate of the auricular movement, the absence of absolute regularity and the great reduction of the auricular muscular movement when compared to the normal, demonstrate, however, that this portion of the curve cannot be interpreted in this way. In the earlier portion of the curve (beats 2-7) the auricular inco-ordination is more clearly visible, but here also a complete analysis of the electrocardiogram is possible by exact fixation of the instants at which the individual auricular and ventricular movements fall. The curve as a whole is a complex picture composed of an accurate super-imposition of R and T variations, the result of ventricular systoles, and of auricular variations, marked P^1 to P^{18} . It would seem that the oscillation appearing in auricular fibrillation is the total result of the electric changes occurring in the individual fibres, and that similarly the movement of the myocardiograph lever is the total result of the combination of contractions and relaxations of the individual fibres. If at any given time a greater number of fibres are in contraction than there are fibres in relaxation, and such a state would be anticipated when the auricle is tending to return to a normal or co-ordinate

* Speaking of the coarser oscillations only.

mechanism, then a tendency to general contraction of the chamber as a whole, and an inclination for the electric variations of given direction to superimpose and produce a more or less prominent resultant curve would be present. There is evidence of a similar kind (which has been referred to in a former communication) in the case of fibrillation of the ventricle and the similar oscillations which are the outcome of it.

The location of the electric change in the auricle is a simple matter if direct leads are taken from the heart itself, and from various parts of the body wall. The oscillations are maximal when the lead is from the auricular substance (Fig. 31 *I* and *II*), and their amplitude decreases according as the distance separating auricle and electrode is widened (Fig. 31 *V* and *VI*). Curves taken from the ventricle direct show comparatively little trace of the oscillations while the auricle is fibrillating (Fig. 31 *III*).

There is therefore no question but that, in experimental auricular fibrillation, oscillations in the electric curve are produced which may be definitely located as arising in the auricle: there is equally no doubt that the oscillations are produced as a result of the fibrillation, for they are contemporaneous with it and with no other mechanism.

It is only at the time when this communication is arriving at completion, that the preliminary notice of Rothberger and Winterberg's researches has come to my notice. The curves which they give as illustrating auricular fibrillation in limb leads are of the same nature as those portrayed by the accompanying figures.

The electrocardiographic curves compared in more detail.

One of the outstanding features in the electric curves of both the clinical condition and experimental fibrillation is the presence of oscillations. These oscillations vary considerably in form, in rate and in extent from case to case, and from experiment to experiment. But when the material for selection is abundant it is often possible to choose from the compares examples of curves which are alike pictorially. Collectively the curves fall into line rather in virtue of qualities which they bear in common.

Rothberger and Winterberg, making independent observations, have recently drawn attention to the oscillations in auricular fibrillation, and have noticed the resemblance of the oscillations found to those seen in cases of irregularity of the heart.

For purposes of pictorial comparison two curves have been selected, and are shown in Figs. 22 and 23. The first is an experimental curve, and the second is from a case of mitral stenosis with completely irregular pulse. The similarity is striking. In instances where the ventricular beat is rapid (Fig. 15), and where on this account the oscillations are obscured, the nature of the rhythm is identified not so much by searching for oscillations as by noticing the deformity of those portions of the curve which lie between the

adjacent peaks R R. The pieces of curve referred to show no resemblance to each other. A similar example but an experimental one is shown in Fig. 17 (the last half of the curve). The first half of this curve represents the escape following vagal stimulation. The oscillations which are so completely unmasked by the prolongation of diastole escape attention in the succeeding cycles. In the clinical curves the peak R is exaggerated, as compared to the normal. The same remark applies to most experimental curves (the comparison may be made in Figs. 20 and 21 and in Fig. 29). The difference is also present in curves taken direct from the ventricle (Fig. 31 *III* and *IV*).

Again, there is the fact that in experimental as well as in clinical curves the general character of the ventricular complex is unaltered. In the dog this can be readily demonstrated by leading from any two points of the ventricular surface. The same type of curve is yielded whether the auricle is fibrillating or in co-ordinate contraction. Fig. 31 *III* and *IV* may be compared. The former, taken while the auricle is fibrillating, shows a faster heart beat to the right and the last phases of the shorter cycles are curtailed. To the left of the same figure, the full complex is shown while the heart is escaping from the inhibitory slowing. The ventricular complexes are of the same form as those exhibited while the sequence is normal, and the heart regular (Fig. 31 *IV*). The same fact may be shown when the oscillations lack prominence. Leads from the upper and lower part of the chest of the same animal gave similar and normal ventricular curves with one or other mechanism present (Fig. 31 *V* and *VI*). The two illustrative curves show the same events, the passage from fibrillation to normal sequence, but in *VI* the galvanometer was arranged to give an excursion approximately three times as great as in *V*.

The electrocardiographic curves, experimental and clinical, are alike in every other respect. The irregular distribution of the ventricular peaks R, the direction of these peaks (direction of base negativity) and the submerged variation T, are features held in common. There is a further characteristic, which deserves more attention. It is common to both clinical and experimental curves. There is no fixed relationship between the heights of the peaks R, and either the pauses which precede them or the height of corresponding carotid beats. The absence of both relationships is shown in Figs 15 and 17. The same disproportions are seen in the condition known as heart alternation*, and it is not improbable that a common factor aids in its generation under the two sets of circumstances. But though I believe a phenomenon of this sort plays some part, yet in certain of the records it is obviously a minor factor. It will be clear that when the oscillations are extensive in amplitude that much will depend upon the relative positions of peak R and summit of auricular oscillation. The individual oscillation may be regarded as **Λ** shaped; if a peak R falls where the depression between

* Winterberg⁷⁷ has reported some observations from which he concludes that fibrillation leaves behind it, on terminating, a state of altered contractility.

two adjacent oscillations occurs, that peak will be relatively short : if it falls on the summit its height will be enhanced : while falling on the side of the Λ a midway position may be expected. Evidence for this view was advanced in the discussion of Fig. 29, and a careful examination of Figs. 22 and 23 substantiates it. The oscillations in these two figures are not spaced with absolute regularity, but it is possible to reconstruct those oscillations which are distorted by R variations coinciding with them. It is found that where a peak R falls at a point at which the summit of an oscillation is to be anticipated the peak is tall in comparison to one which falls where a depression is expected. On the other hand there are many curves in which this explanation is insufficient. Fig. 31 *III*, is an experimental curve taken by means of direct leads from the right ventricle during fibrillation. Oscillations are entirely absent, yet there is the absence of relationship between the amplitude of preliminary variations and the length of preceding pause.

Reviewing the electrical phenomena as a whole it becomes manifest that the clinical and experimental curves resemble each other in every respect. The close pictorial resemblance in many instances, and the absolute identity of all the essential characteristics taken alone or in relation to corresponding events, are in themselves sufficient to carry conviction of a similar mechanism in clinical and experimental instance.

The radial curves compared.

In 1906, Cushny and Edmunds⁸ investigated a case of paroxysmal irregularity of the heart. Unfortunately no venous curves were taken, but from the radial tracings it is in the highest degree probable that the irregular heart action with which they were dealing was of the nature here considered. These authors drew attention in their paper to the close similarity of the radial curves taken from their patient and arterial curves obtained from dogs in which the auricle was in a state of fibrillation. They remarked in particular upon the absence of relationship between the height reached by the arterial beats and the pauses preceding them.

In so far as the experimental arterial curves are concerned, I have little to add to the description given by Cushny and Edmunds. The irregularity of the arterial pulse in auricular fibrillation is absolute and has the same qualities as those presented by the curves in complete irregularity of the heart in man. The rate of the ventricles is increased. Some examples of the Hürthle manometer curves taken from the carotid of a single animal are given in Fig. 6. A short strip of normal curve, the only piece in the figure, is shown in the third line. At the point where the arrow is placed, the auricle, which had spontaneously ceased to fibrillate, was taradised once more and the fibrillation was re-induced. The curves were taken with the chest wall intact and may be compared with the numerous radial tracings given in this paper (Fig. 1, etc.).

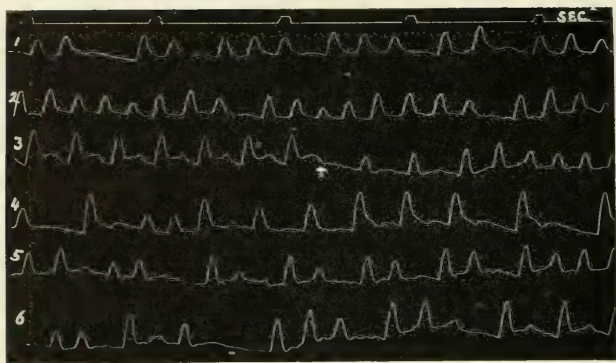


Fig. 6 (1-6). $\times \frac{1}{4}$ linear. The time marking is in seconds. Hürthle manometer curves from the carotid of a dog in which the auricle was fibrillating. Chest wall intact. A small portion of normal curve is shown in line 3. At the point where the arrow is placed the auricle, which had resumed its normal rhythm, was faradised.

The venous curves and their comparison.

The venous curves associated with complete irregularity of the heart have been discussed at length in the preceding pages.

The venous curves in experimental auricular fibrillation were obtained by exactly similar means*. The ink polygraph was employed, and large and well-fed dogs were chosen for the purpose. The femoral curves were secured by exposing the artery in the thigh and by stitching the receiving apparatus in place over it. The jugular tracings were obtained by fastening the receiver to the shaven neck; the application of vaseline ensured complete closure of the transmitting system. Curves have been taken with the chest open and closed. They present no essential difference; those which illustrate this section are examples from animals in which the chest wall had been restored.

In Fig. 7 *a* and *b* strips of curve from a single animal are represented. In the upper curve the normal rhythm is interrupted by a short induced paroxysm of irregularity due to fibrillation of the auricle. The venous tracing while the rhythm is regular, before and after the paroxysm, consists of clearly inscribed *a*, *c* and *v* waves. During the paroxysmal period each of the irregular beats (several fail to impress the femoral curve) is accompanied by two prominent waves in the veins; the waves are separated from each other, and the second wave is succeeded, by a well-marked depression.

* Hering²⁰ states in a recent note, that he has seen venous curves, and that they are of ventricular form.

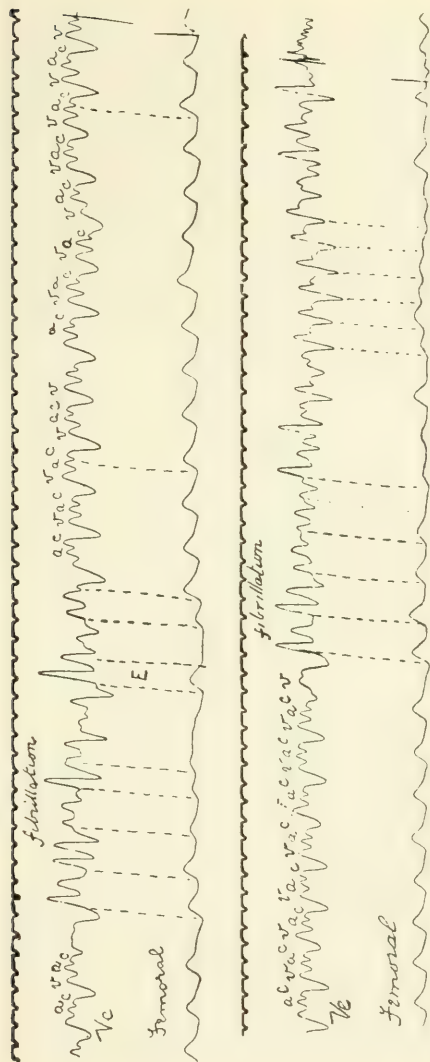


Fig. 7 *a* and *b*. Polygraph curves taken from a dog with the chest wall intact. Venous and femoral curves are portrayed. Each curve shows the normal rhythm, associated, with a_c , v_c and v waves, interrupted by a short paroxysm of irregular tachycardia, as a result of faradisation of the auricle. During the paroxysm the venous pulse is ventricular in form.

The main waves fall in the systolic interval. E, but where the pause of diastole is long a stasis wave is also apparent. The lower tracing of this figure shows the onset of a similar paroxysm, and the venous curve at its commencement is of the same type. Towards the termination of the curve there is a succession of more rapid beats and the corresponding venous curves incline to the plateau form: the systolic depression of the slower beats is wanting. At no point in either tracing are true presystolic waves discoverable while the auricle is fibrillating. The venous records are of precisely the same type as those which characterise the clinical condition. The figures may be compared most profitably with Fig. 2 B and A, and with Fig. 4 B (experimental venous curves, abnormal and normal, are also shown in Figs. 20 and 21). The variation in form with the enhanced rate of ventricular beats has its clinical parallel. Further, in the experience of these experiments, variations have been met with which seem to indicate that the plateau type of venous curve may result from cardiac dilatation, but this feature has received no special investigation. The plateau form is more commonly found towards the end of an experiment. The examples given in Fig. 8 belong to the later stages of an experiment.

Fig. 8 is published to illustrate the effects of vagal stimulation. Irritation of the vagus, while the auricle is in delirium, produces very definite effects. By inspection of the auricle it is determined that the muscular activity is more finely subdivided and more flickering during the time of inhibition. The auricle is more ballooned. At times the fibrillation ceases altogether (Kronecker and Spallitta²², Phillips^{18, 19}). In my experience the cessation of the delirium, and the return of the normal sequence under vagal stimulation is almost invariable, provided that the fibrillation has been of short duration. But the result is not absolutely constant, and it is less frequent when the inco-ordinate movement has been present for many minutes. The increased distension is invariable. The ventricular rhythm is always markedly retarded (K. and S.), and the rate of beat is slow for some while after the cessation of the stimulation. As the heart quickens again it may do so in response to a fibrillating or to a normally contracting auricle.* When an auricle has been fibrillating uninterruptedly for some while, and the vagus has been stimulated and slow ventricular action has resulted, I have noticed, by no means infrequently, that after the cessation of stimulation and with the re-establishment of rapid response to fibrillation, the latter having continued for a brief period only, gives place to normal or co-ordinate contraction. The retardation of the ventricular beat, while the auricle is still fibrillating is probably due, as Cushny and Edmunds suggest, to a hindrance to the passage of the auricular impulses across the auriculo-ventricular junction. Both the curves which are given in the accompanying figure (Fig. 8) show a return to the normal rhythm

* According as the inhibitory influences have or have not re-established the predominance of the normal pace-maker.

after a period of ventricular slowing. But in each instance a greater or lesser grade of A-V heart-block is demonstrated by the venous curves, after the restoration of the usual sequence. In the upper tracing the *a-c* interval is wider with the first few beats and gradually diminishes up to the point where the stops are seen. The heart-block is of a higher grade in the second tracing. At the escape of the auricle from its fibrillary state it meets with no ventricular response, and during the rest of the figure a 2 : 1 relationship of auricular and ventricular systoles is maintained. The definite sign of obstruction to the passage of auricular impulses and the halved ventricular rate which results in the later stretches of the curve, strongly favour the view that during the fibrillary period the slowing has been brought about in a similar manner, namely by a reduction of the number of impulses conveyed from the upper chamber. Subsequently, the clinical import of these remarks will be more manifest.

The duration of the fibrillation is clearly depicted in the figure. As soon as the pulse rate falls and the diastolic pauses reach an appreciable length, fine oscillations following each other at a rate of approximately 700 per minute make their appearance in the venous curves. They are produced by the fibrillary movements of the auricular wall and vanish at the return of the co-ordinate contraction of its musculature (thus, in the upper tracing the fibrillation ends at the spot indicated by the arrow)*.

The appearance of these rapid and small undulations of pressure in the veins during experimental fibrillation finds its parallel in the clinical case. The waves are not found in all cases, experimental or clinical; a slow ventricular action is essential (cp. Fig. 4 A. and the discussion relating to it). While their dependence upon fibrillation in the experimental case cannot be gainsaid, a similar origin is not demonstrated with equal facility in the clinical instance. At the same time an additional observation is helpful. In man the rate of the venous waves is approximately the same as the rate of the electric oscillations. Simultaneous electric and venous curves are shown in Fig. 19. The oscillations are clear in both lines, and the rate is approximately 450 in each. The rate as portrayed by this figure may be compared with that found in Fig. 4 A. a curve obtained from the same patient on the same day. A comparison between the rates of the experimental oscillations and the experimental venous undulations in the figures already described is not practicable, for the vagal stimulation alters the character of the fibrillation. To the naked eye and in myocardiograph curves the movement appears finer and faster during inhibition. The electric oscillations are also more rapid under these circumstances (see Fig. 17, in which the rate is approximately 800 per minute). In many instances the rapidity is even greater. I have tried on several occasions

* In the lower tracing, the fibrillation ends in what appears to be a full auricular contraction. I have seen the same in electric curves; it has probably taken place in Fig. 31 II; such beats usually yield anomalous electric curves, and are not the outcome of sinus impulses.

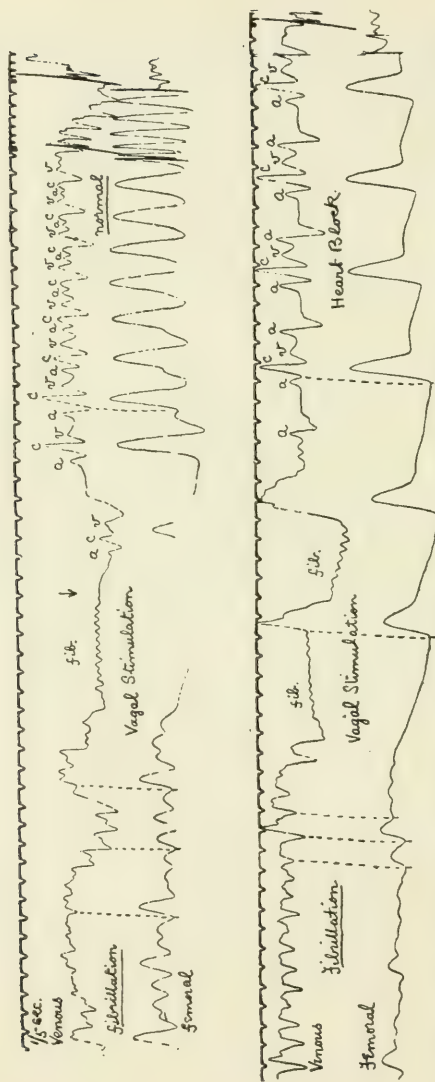


Fig. 8 a and b. Polygraph curves from a dog. Chest wall intact. Showing the venous and femoral curves while the auricle is fibrillating. During each record the vagus was stimulated. Fibrillation waves in the veins are unmasked and eventually the fibrillation ceases. With the return to the normal rhythm a certain degree of heart-block is present.

to institute a less precarious comparison by severing the auriculo-ventricular bundle, in the hope of obtaining simultaneous venous and electric curves while the ventricular beat is slow and the oscillations prominent, but so far the experiments have lacked success.

It seems plausible to attribute the finer state of fibrillation under vagal stimulation to the phenomenon assigned as the cause of the slowing of the ventricle, namely, to heart-block, at the A-V junction in the one case, and in the walls of the auricle in the other. A conclusion which seems warranted and which is more relevant to the main thesis of this communication is that the venous and electric oscillations, be they clinical or experimental, are the result of one and the same mechanism.

Reviewing the observations upon the venous pulse in complete irregularity of the heart and in experimental auricular fibrillation we may state that the records are alike in every respect.

A summary of the comparison instituted between the records obtained in complete irregularity of the heart in man, and in experimental auricular fibrillation.

In an earlier section it was stated that the proposition advanced, namely, that the two conditions, complete heart irregularity in man and auricular fibrillation in the dog are of one and the same nature, must stand or fall by a careful comparison of the two conditions. This comparison has been completed in the intervening sections. It has been ascertained that the clinical and experimental conditions resemble each other in every respect in which they have been investigated. The observations are summarised in the following table, which consists of a systematic list of the features presented in common.

The radial curves.

1. *Rate increased as compared to the normal.*
2. *Presence of absolute irregularity.*
3. *Absence of fixed relationship between the strength of a beat and the preceding pause.*
4. *The presence of many "dropped" beats, and of beats of all shapes and sizes.*

The venous curves.

1. *The presence of the ventricular form of venous pulse (the absence of "a" waves).*
2. *The appearance of definite variations in the form of the individual venous pulse curves.*
3. *The presence during diastole of rapid undulations of venous pressure when the heart beat is slow.*

The electrocardiograms.

1. *The occurrence of a base negative variation R at the commencement of ventricular systole.*
2. *The presence of a variation T which is deformed in leads from the extremities, but which is clear cut and of normal form in leads from the heart itself.*
3. *The absence of an auricular systolic variation P.*
4. *The occurrence of continuous oscillations, generated in, or in the vicinity of, the auricle. The rapidity of the oscillations. Their disappearance when the normal rhythm is resumed.*
5. *The absence of fixed relationship between the height of the peak R and the length of the preceding heart pause. The absence of relationship between the height of R and the height of corresponding arterial curves.*
6. *The increase in the size of R as compared to the similar peaks of the normal curve.*

AURICULAR FIBRILLATION AS A CLINICAL ENTITY.

The clinical and experimental comparison employed as a deliberate test of the proposition, originally based upon purely clinical facts, is invaluable. Without it our attitude towards a large group of clinical cases remains in the hypothetical stage. With the comparison hesitancy gives place to a feeling of security, and we may approach our patients with a true appreciation of the affection which we so frequently encounter. The meaning of many otherwise obscure manifestations becomes clear, and we are in a position to pursue the path of investigation towards the hoped for cure or prevention with the sense of a firm footing.

The possibility of the occurrence of auricular fibrillation as a clinical phenomenon has been recognised by several writers. As we have seen, it was suggested by Cushny and Edmunds.* Their suggestion, based as it was upon the comparison of the arterial curves in a single clinical case with those obtained experimentally, has not developed up to the present time; the hypothesis was a tentative one. In the discussion at the end of their paper they state: "Of course we cannot claim to have shown definitely any connection between this type of irregularity in the dog's heart and that in the case described. At the same time there exist similarities between them, and the sudden onset of the irregularity in each case suggests a common cause;" Wenckebach¹⁵, writing a year later, briefly discussed the possibility.

In 1908, Hirschfelder²¹ published some notes on auricular fibrillation, and concluded that certain cases of paroxysmal tachycardia were the result

* The first suggestion came from Cushny (*Journ. Exper. Med.*, 1899, IV, 340).

of increased auricular irritability. The auricular tachycardias to which he refers are of an essentially different nature to the disturbance of heart rhythm which we are discussing, and there is no reason to suppose, but on the other hand every reason to deny, that they are the result of auricular fibrillation in the true sense of the term. But when the auricle is faradised with a weak current, a preliminary quickening of rhythm takes place, and as the stimulus is increased and spreads fibrillation may ensue. In this limited sense a connection may be traced between regular auricular tachycardias and auricular fibrillation, and I have met with a single instance in which the one condition (regular auricular tachycardia) passed directly into the other (complete heart irregularity or auricular fibrillation). (This instance is subsequently described: Fig. 9 and explanatory remarks*.)

It may be said, therefore, that although auricular fibrillation has been regarded by certain isolated observers as a possible phenomenon in clinical pathology, its association with anything beyond rare cases of paroxysmal tachycardia has not been seriously attempted until the last few months. The introduction of the string galvanometer as an aid to diagnosis has facilitated a much wider conclusion. While these investigations were in progress this conclusion has been partially and independently arrived at by Rothberger and Winterberg⁶⁶, working in Vienna. In their preliminary communication they conclude that certain cases of *pulsus irregularis perpetuus* are due to fibrillation. A large clinical experience of such cases exempts me from the necessity of restricting my conclusions, and permits me to assert that all such cases belong to a single group, and that the mechanism is the same in all.

Where, in conjunction with an absolutely irregular pulse, the ventricular form of venous pulse and the characteristic electrocardiogram are present, the evidence is complete. But, as in a large number of patients no case, exhibiting complete irregularity and the ventricular form of venous pulse, has been found, which does not show likewise the typical electric records, the electrocardiograms cannot be held as essential to the diagnosis. Moreover, as no case of complete irregularity has been met with, or has been recorded by any other writer, in which the venous pulse when given may not be interpreted as of the ventricular form, and as the cases in which these venous and arterial signs are present together have been published in abundance, the conclusion may be carried a stage further. There is no hesitation in stating that in the vast majority of cases of complete irregularity of the heart, auricular fibrillation is responsible for the disturbance of ventricular rhythm. It is sufficient if a single strip of curve is obtained from the radial artery, and if no two beats on the strip are of the same length (and given, of course, that the heart rate is not manifesting a gradual acceleration or retardation while such a strip of curve is recorded) then the statement that auricular fibrillation is present is justified in all but extremely

* Hewlett⁶⁷ has reported a case which was very possibly of the same nature.

exceptional cases*. It may be affirmed that auricular fibrillation accounts for the largest class of persistent heart irregularities: a class which, broadly speaking, composes 50 per cent. of all such irregularities. And in dealing with cases of mitral stenosis admitted to hospital with failing compensation, it may be said that the presence of auricular fibrillation is the rule.

In discussing the question of the possibility of auricular fibrillation, I have been frequently met by an argument of a purely *a priori* nature: and, judging from the note by Rothberger and Winterberg, these observers appear to have had a similar experience. It is said that it is inconceivable that the heart should remain in this state for long periods. It should be known that Janowski¹⁰ recorded a case of complete irregularity of 5½ years' duration, and Mackenzie has watched similar patients for even double this time. In reply Rothberger and Winterberg instance the persistence of tremor in the tongue following nerve section, and I may draw attention to the well-recognised and chronic fibrillary twitching of the voluntary musculature in many nervous maladies†. Fibrillation of the ventricle it is true is accompanied by almost instant dissolution, but fibrillation in this chamber brings the circulation to a prompt standstill. The auricles are not indispensable to the circuit of blood in the body, but may be regarded rather as temporary reservoirs which accommodate the blood flowing to the heart while the ventricle is in systole. The large veins are perfectly capable of subserving this function, and the resulting general disturbance of the circulation is but slight. We have perfectly definite evidence that the normal auricular contraction is in abeyance in a large number of patients in whom the peripheral circulation is unhindered, and auricular fibrillation may last for many hours in a dog and yet the blood-flow in the body is fair throughout. Therefore, on the ground that auricular fibrillation is incompatible with a continued circulation, this argument may be entirely dismissed. If it is implied that the hindrance would occur, not in the auricle, but in the ventricle in virtue of the high grade of disorder of the rhythm, it may be replied that such an argument is but a denial of an ascertained fact. The secret of the lack of disturbance as

* The only exception, I think, is the rare case of gross sinus arrhythmia, independent of respiration.

† I had hoped to have obtained direct evidence upon this aspect of the question, but no opportunity has presented itself. I am convinced that a similar affection is found in the lower animals, and have seen one example of it. Examination of the heart *in vivo* was not practicable: sooner or later, it is hoped, observations in this direction will be forthcoming.

Since these pages were written a horse has been obtained, through the kindness of Professor Woodruff of the Royal Veterinary College, in which electrocardiographic curves demonstrated complete irregularity and an absence of P variations. The horse was killed and the chest quickly opened. Unfortunately the right ventricle was damaged during this operation. Inserting the hand into the chest the ventricle could be felt to beat rapidly and irregularly. No movement could be felt in the right auricle. The ventricle was grasped and drawn through the wound, but fibrillation ensued. The auricle was then seen in a state of fibrillation, and it continued to fibrillate until all movement ceased. The necessary repetition of this observation will be undertaken so soon as opportunity presents itself.

a result of the condition *per se* seems to me to be found in the direction of propagation of the wave of contraction in the ventricular musculature. The electric records testify that the contraction route taken is the normal route. Strong and weak contractions may be mixed together in profusion, but all the beats will tend to be effective in expelling the ventricular contents, and the majority of the beats are effective.

Even if the *a priori* arguments could not be met, the evidence for the proposition is so positive that we should be justified in setting them aside. A case is recorded in this communication (CASE 12), in which incontrovertible evidence (arterial, venous and electric) is at hand to prove the presence of the fibrillation: and, be it noted, this case has been under observation, and has presented the same mechanism, as shown by arterial and venous curves, for a space of five years.

AURICULAR FIBRILLATION AND HEART-BLOCK: THE ACTION OF DIGITALIS.

It is by no means uncommon to meet with clinical cases of complete irregularity in which the ventricular action is not excessive, and instances are not infrequent in which the rate is actually reduced. Moreover it is well known that in complete irregularity of the heart retardation of the ventricular rate constitutes one of the most characteristic actions of drugs of the digitalis group. In consideration of the fact that the sinus rhythm is in abeyance the cause of the slowing must be sought in a part of the musculature other than that at which the pace-maker is situate.

In discussing the experimental venous curves, the question of ventricular slowing under vagal stimulation received attention, and facts were brought forward in favour of the contention that the retardation is the result of the blocking of fibrillation impulses at the A-V junction.

Now we have proofs that digitalis acts upon the vagus and that the vagus has a powerful influence upon A-V conduction. Further, we have very suggestive evidence that digitalis may act *directly* upon the junctional tissues between auricle and ventricle. The facts upon which these conclusions are based have been recently examined in a communication to the *Quarterly Journal of Medicine*²⁰. Their relevance to the phenomenon of ventricular slowing in clinical fibrillation should be obvious: it may be surmised that digitalis slowing is produced either by a direct action of the drug, or by an indirect action through the vagus, upon the junctional tissues. We may examine the remaining evidence which supports this view.

We know that in rheumatic heart affection, and in mitral stenosis in particular, it is common to find signs of imperfection or conduction of the contraction wave from auricle to ventricle (see CASE 11 and 12), and we are also aware that in such cases it is the rule that the exhibition of digitalis or allied drugs enhances the grade of heart-block (Mackenzie²⁰ and others). We know further, as a result of Mackenzie's work, that of cases of auricular

fibrillation ("nodal rhythm"), those which are of rheumatic origin or those in which mitral stenosis is present are most susceptible to digitalis. Therefore the suggestion which is put forward is that the slowing of the heart, when auricular fibrillation is present and digitalis is given, is due to an increase of a previously existing defect* in the conduction to the ventricle of those impulses which are built up rapidly and irregularly in the auricle. We require facts from two sources in confirmation of this view. First, experimental data are necessary, and at present these are not forthcoming. Secondly, we require more extensive observations which will show rather than suggest that, in those cases of fibrillation in which digitalis produces retardation, conduction was impaired before the onset of the new rhythm. Or, more strictly perhaps, it will be necessary to show that conduction was primarily impaired in a much larger percentage of cases which react than of cases which fail to react, for it is possible that fibrillation may be the forerunner of conductivity changes in some instances. These statistics will be slow in coming, but already there are indications in harmony with the proposition. It is the rheumatic case which usually reacts, and it is the rheumatic case which usually shows altered conduction. Again, taking the cases which are recorded in this paper, three of the patients observed before the onset of fibrillation, or during the intervals between paroxysm, have been thoroughly tested from this point of view. Two of the cases (CASES 2 and 10), in which the a-c or P-R intervals were of normal length during the normal sequence, failed to react†, while the third, a case (CASE 11) in which conductivity was definitely impaired, reacted in the most typical manner.

We have seen that two allied phenomena, increased heart-block when the A-V rhythm is present and retardation of the ventricular rate in auricular fibrillation, may occur as a result of digitalis. A similar parallel may be drawn between heart-block arising in the absence of drug administration and the spontaneous slowing which not infrequently occurs in complete irregularity. Moreover cases are on record in which the irregular rhythm is slow from the outset. A number of patients with slow and irregular heart action have been collected and described recently by Mackenzie¹⁰ under the term "nodal bradycardia," and they form an extremely interesting group. The examination of one or more such cases with a view to ascertaining the nature of the auricular action became crucial. As a result it has been found that auricular fibrillation is present in these instances also; the two cases examined may be cited. The details of these patients are most instructive, but they can be alluded to but briefly. Both cases belong to the series reported by Dr. Mackenzie, and I am indebted to him for the opportunities of re-examining them. Fuller clinical reports will be found in his communication to *this Journal* (p. 23).

* The defect may be a potential one in certain instances.

† Digitalis was administered until sickness resulted.

CASE 12. The following is an abstract of the original report (*Heart*, Vol. I, p. 25).—W. H., a subject of rheumatic fever, was known to have had impairment of conduction in greater or lesser degree for 12 years. He then suddenly developed slow and irregular action of the heart and demonstrated the ventricular form of venous pulse. In this state he continued a week, at the end of which time the pulse was again regular and the *a-c* interval was 0.4 sec. in length*. Seven months later the same slow and irregular action of the heart was resumed and it has persisted until the present time, a period of five years.

A tracing from this patient is given in Fig. 4 A. On the day upon which he came for re-examination the pulse rate was 49-68. The pulse was absolutely irregular, the venous curve being of the ventricular form. There were fibrillation waves in the curves. In Fig. 19 simultaneous electrocardiographic and venous curves are shown. The electrocardiographic record is characteristic and the usual oscillations are present.

There can be no question but that the case is one of auricular fibrillation. The long-continued history of heart-block previous to the onset of the irregularity and its presence during a brief interlude strongly supports the view that the slow ventricular rhythm resulted from the known inefficiency of the junctional tissues which transmit the irregular impulses formed in the auricle.

CASE 13. M. M., age 45 (extract from *Heart*, Vol. I, p. 33).—"Permanent nodal rhythm, bradycardia associated with mitral stenosis. Occasional attacks of syncope and convulsions."

Recently the case has been fully re-investigated, and a detailed report of it will be found in the contemporary number of the *Quarterly Journal of Medicine*. The main facts in regard to the patient are as follows:—Apart from the epileptic seizures the pulse rate is almost constantly at or about 30 per minute. This is the rate generally assumed by the ventricle when it is entirely dissociated from the auricle. As in complete heart-block the pulse is *regular*. The patient has syncopal and epileptic attacks in every way similar to those met with in the subjects of complete heart-block. Extrasystoles, when they occur, are followed by pauses equal to the spaces between adjacent beats of the usual slow rhythm. The patient has had syphilis.

Briefly, the patient presents a picture identical with that of complete heart-block, as usually recognised, in every respect but one. There are no co-ordinate auricular contractions. The venous pulse is of the ventricular form and electrocardiograms from the extremities and chest wall (Fig. 18 and explanation) afford clear evidence that the auricles are fibrillating.

The conclusion is unavoidable that the case is one of complete heart-block (the result of syphilis) and auricular fibrillation. The regularity of the pulse is a natural consequence of the inability of the auricular impulses to reach the ventricle. Fredericq⁹ has shown experimentally that section of the bundle, while the auricle is fibrillating, cuts off all auricular impulses.

Dr. Gibson, of Edinburgh, has drawn my attention to a case, of considerable interest in this connection, which he reported in 1906. The tracings

* The normal *a-c* interval is 0.2 sec. or slightly less.

obtained were those of incomplete heart-block (the auricular rate was 168 and the ventricular 42). On one occasion there was a temporary disappearance of the auricular venous waves, and *while the pulse became completely irregular, though still phenomenally slow, faint and rapid oscillations appeared in the venous curve.* (The rate of the oscillations was approximately 375 per minute, as shown in the published curve¹¹). A post-mortem revealed an increase in the fibrous tissue of the bundle with wide separation of the fibres constituting it*.

I think there can be no reasonable doubt that here also auricular fibrillation and heart-block were present in combination, and the most important evidence for it is the *type of irregularity* which the pulse assumed when the regular auricular waves vanished.

Reviewing the three preceding cases we may conclude that auricular fibrillation occurs clinically in association with heart-block, either partial or complete. The case for a similar mechanism under digitalis is strengthened. And I would go further and put forward the general hypothesis that when auricular fibrillation is present and a slow ventricular action is found, whatever its cause, a certain degree of temporary or permanent impairment of the functions of the junctional tissues may be assumed.

A tabulated statement of the suggested or proved relationships between heart-block and auricular fibrillation may be given in summing up the conclusions of this section.

| A-V RHYTHM. | | AURICULAR FIBRILLATION. | |
|------------------------------------|---|---|--|
| <u>Heart-block.</u> | <u>Digitalis H. B.</u> | <u>Heart-block.</u> | <u>Digitalis H. B.</u> |
| <i>Lengthened a-c interval</i> | <i>lengthened a-c interval</i> | <i>spontaneous slowing of irregular tachycardias</i> | <i>ordinary digitalis slowing</i> |
| <i>2:1; 3:1, etc., heart block</i> | <i>2:1; 3:1, etc., heart block (Mackenzie¹²)</i> | <i>spontaneous slowing of marked grade, and cases with onset of very slow and irregular rhythm (CASE 12 and Gibson's patient)</i> | <i>marked slowing on digitalis (Mackenzie¹³)</i> |
| <i>Complete heart-block</i> | <i>complete heart-block†</i> | <i>auricular fib. and complete heart-block (CASE 13)</i> | <i>digitalis slowing with the production of a regular pulse of 30-40 per minute ("Heart," Vol. I, p. 39)</i> |

* I may add that Dr. Gibson writes me that it occurred to him at the time that the auricles might have passed into fibrillation. A somewhat similar case has been reported by Herxheimer and Kohl (*Deutsch. Archiv f. Klin. Med.*, 1910, xcvi, 330), but the facts, I believe, have been misconstrued.

† Tracings from a case of temporary complete heart-block the result of the administration of strophanthus were shown to me lately by Dr. Emanuel of Birmingham.

THE CAUSE OF THE ONSET AND DURATION OF AURICULAR FIBRILLATION.

The primary object of this paper is to establish the fact that auricular fibrillation is a frequent clinical affection. Once established our duty lies in the direction of seeking its cause. In this respect I am unable to offer more than incomplete evidence, and the views expressed are at present almost purely hypothetical.

It will be generally allowed that fibrillation consists in the elaboration of numerous and fresh impulses in the auricular walls. It may be regarded as a state in which stimuli are generated, at many separate and uncertain points and the inco-ordination of the contracting fibres may be held to result from the impact of contraction waves and the production of localised areas of block. The condition may be compared in many respects to the confusion of uncontrolled traffic in a crowded thoroughfare. In seeking for an explanation of the origin of auricular fibrillation we naturally turn to our knowledge of the causes which originate new impulses. That, at the present time, is the most important problem relating to cardiac irregularities.

Now it has been shown that an increase of intracardiac pressure is succeeded by the appearance of ectopic impulses. Hering¹³ employed this method in his studies of extrasystoles. Auricular fibrillation is specially prominent in cases of mitral stenosis; the high intra-auricular pressure in this disease might be considered sufficient to account for its occurrence. I have observed the onset of auricular fibrillation in experiment on several occasions when, by pressing on the abdomen, the venous inflow was suddenly increased. But the difficulty of accepting the view as a general hypothesis is obvious, for auricular fibrillation occurs in many cases in which a raised auricular tension may not be assumed.

A purely mechanical doctrine is untenable. The cause must be sought in a more detailed study of the morbid anatomy, and attention should centre in the auricular walls. So far we have little information. Several cases of gross irregularity of the heart were investigated by Radasewsky¹⁴ some years ago, and he found widespread fibrosis of the heart. He remarked that the damage was most extensive in the auricles. Mackenzie¹⁵ has given post-mortem notes of eight cases of "nodal rhythm": in three the auricle showed fibrosis, in two reports it was not mentioned, in one not examined, in one the septum was "stretched," in one atrophied. The ventricle, on the other hand, showed fibrosis in seven instances: in one it is not mentioned: in six of the cases the junctional tissues were fibrosed or otherwise damaged. It is obvious from the accounts that the node of Tawara and the bundle received more attention than the rest of the heart. Schönberg¹⁶ has recently examined five hearts from patients with persistent irregularity: in one case venous and radial curves are available¹⁷, and from his clinical accounts the remainder were probably of the same nature, namely, complete irregularities. He found a chronic inflammatory (lymphocytic) infiltration of the tissues at the junction of superior cava and auricle in all. He asserts that

this was the chief lesion; but here again it is obvious that attention has been concentrated upon a limited portion of the musculature. Amongst the cases belonging to this investigation one only has come to autopsy. It was a case of streptococcic endocarditis, and a large area of ulceration was found on the septal wall of the left auricle. I have since seen, through the kindness of Major-General F. Smith, a case of irregularity in a horse. The irregularity was complete, as shown by tracings, and a systolic pulsation was apparent in the veins of the neck and reached the angle of the jaw while the animal was standing. Great breathlessness and dropsy were present. The disturbance of the heart's rhythm was of eight months' duration. An examination of the heart showed considerable hypertrophy of the ventricles and auricles: it was especially marked in the latter. The endocardium of the left ventricle and auricle was opaque and thickened: there were large and scattered patches of sub-pericardial fibrosis in the left auricle, but in no other part of the musculature. (The histology will be reported at a later date.)

It is possible that fibrosis, by interfering with the circulation in restricted areas of the musculature, sets up a state of irritability. The tendency for anæmia of the muscle to bring about new impulse formation is readily demonstrated experimentally. Ligation of a branch of a coronary artery is usually followed by the appearance of extrasystoles^{30b}. But it is difficult to suppose a constant state of anæmia in the affected tissues, and an anæmia of long duration. It must also be remembered that extensive fibrosis may occur without irregularity⁴⁷.

Some light seems to be thrown upon the question by an examination of the relation of fibrillation to extrasystoles.

There appear to be two types of case of the paroxysmal affection. A type in which the interludes are characterised by a perfect regularity of the heart (*CASE 10*), and a type in which the regular rhythm of the slow period is interrupted by extrasystoles (*CASES 2 and 11*).

In my own limited experience the extrasystoles which interrupt the slow periods, or those which interrupt the normal rhythm prior to the onset of the fibrillation, have been auricular in origin (*CASES 2 and 11*). Their presence in these patients and in certain of those reported by Mackenzie arrests attention. We cannot divorce the problems of the factors influencing the origin of single and multiple ectopic impulses, neither can we separate these questions from that of the origin of fibrillation. The production of a single new impulse, of a series of impulses from a single focus, or of multiple impulses from scattered foci, is a matter of degree. Furthermore, we cannot exculpate these single ectopic beats. They appear to participate in producing the ultimate crisis. In the cases observed they have been very numerous. In the last number of this *Journal* a case was described in which auricular extrasystoles were as numerous as normal beats, and in this patient paroxysms of ectopic beats were seen, which also arose in the auricle. On one occasion while a paroxysm was in progress the auricle passed into fibrillation: and after its duration for about half a minute the auricular paroxysm reappeared.

A portion of the curve, is reproduced in Fig. 9. To the left is the fibrillation period, and to the right are a few beats of the paroxysm for comparison. The original curve is too faint for publication, but the two sections of curve have been traced by a skilled draughtsman and the original is well portrayed. A stop and two inches of curve have been excised at the point where the vertical line is placed. The change from one mechanism to the other was not recorded.

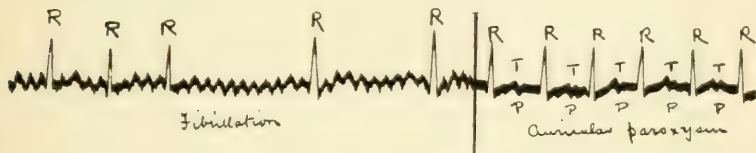


Fig. 9. H. B. (12th Aug. 1909). From a case fully recorded in the last number of this *Journal* (page 262). The original curve has been retraced, and two inches of curve have been excised. To the left the electrocardiograph shows auricular fibrillation. To the right is a paroxysm of regular tachycardia, starting, not at the sinus, but in the auricular walls. This fact is recognised because the auricular variations are absent in their usual form. The peaks R of this paroxysm are not longer than those of the preceding fibrillation period, yet they were always longer than the peaks R of the normal rhythm when the two could be compared. The comparison is utilised as evidence that the peaks R of fibrillation are higher than those of the normal rhythm.

Now in the case of regular auricular paroxysmal tachycardia the actual paroxysms are usually if not always foreshadowed by the occurrence of single or multiple ectopic beats of a different kind. This has been observed invariably in the paroxysms of two cases of auricular tachycardia (*Heart I*, p. 262 and *CASE 15*, with Fig. 26 of this paper). And I have advanced the view that the preliminary beats stand in casual relationship to the paroxysms themselves. If single or multiple beats arising in the auricle may predispose to the production of a paroxysm of regular beats also arising in the auricle, may not these beats also account in part for the onset of an attack of fibrillation? The question arises as to whether a beat arising *de novo* in a chamber of the heart and pursuing an abnormal course in this chamber will enhance the irritability of the musculature in the immediate neighbourhood. Supposing that two or more extrasystoles are started at the same time at different points in the musculature of an irritable auricle, are not those factors present which are calculated to produce a condition of absolute inco-ordination?

The evidence is at present only suggestive; long paroxysms of rapidly recurring beats are apparently provoked by other beats of a similar nature,

but springing from a separate focus (*CASE 15*). The suspicion is awakened that an extrasystole enhances the irritability of the tissues affected, and that their presence in numbers may predispose to if not actually determine the culminating inco-ordination. Furthermore, it is possible that fibrillation, when once produced under suitable circumstances, may itself maintain the increased irritability, and thereby tend to the continuation of the inco-ordinate state. Whether this is so or not should be determinable experimentally, and there are already facts which support an answer in the affirmative.*

Fibrillation is readily produced by faradisation, but after a short period of faradisation the return to the normal rhythm is almost immediate. If the muscle is stimulated periodically and paroxysms of fibrillation result, it is common to find that each successive stimulation gives a more permanent result, that is to say, a result outlasting more and more the actual stimulation, and often a final stimulation will produce a long continued state of inco-ordination. Moreover, the longer paroxysms seem to be less under inhibitory control. Thus it may be held that the fibrillation itself aggravates the irritability of the auricular tissue. It is perhaps a factor of this nature which accounts, partially at all events, for long continued auricular inco-ordination in patients who are affected with it.

AURICULAR FIBRILLATION AND VENTRICULAR EXTRASYSTOLES.

Radasewsky found diffuse areas of fibrosis, not only in the auricle, but also in the ventricle, in cases dying with gross heart irregularity. Mackenzie reported similar changes in "nodal rhythm." Dr. Koch, of Freiburg, tells me that in cases of complete or "chronic" irregularity his experience is similar. We should therefore anticipate that in diffuse fibrosis impulse formation would be frequent in the ventricle. This is actually found to be the case. In the intervals between paroxysmal attacks or before the onset of permanent irregularity, ventricular extrasystoles† have been recorded by Mackenzie. But, as opposed to the possibilities in the auricle there is no reason why co-ordinate ventricular responses to such impulses should not occur when the fibrillation is established. They are not infrequent. An example has been recorded by Hering¹⁸, and in the present series of thirty cases examined electrocardiographically, they were exhibited by seven. They are recognised mainly by the electrical variations to which they give rise, and by the fact that they do not affect the arterial pressure in the same measure as do the ventricular beats which result from auricular impulses.

* It would be of interest to know whether, in cases in which extrasystoles are frequent while the pulse is slow, the periods of irregular tachycardia are of longer or shorter duration than in those patients in whom the slow pulse is uninterrupted in its regularity.

† Analogy would suggest the occurrence of ventricular fibrillation also. Unexpected death in patients with fibrotic hearts is a well recognised fact, and it is not uncommon in patients with auricular fibrillation (*CASE 4*).

A notable example is shown in Fig. 24. The responses to auricle are denoted in the usual way, the first variation is marked R. The remaining beats are ventricular extrasystoles without exception: (the extrasystoles are marked E and the variations are distinguished by letters and figures indicating direction and order, thus *n1* signifies first base negative variation). In the figure none produce an effect upon arterial pressure. Auricular extrasystoles may be placed out of court* while the auricle is fibrillating, and this is clearly demonstrated by the general character of the remainder of the curve and the occurrence of oscillations *ff*.

Considering the variations presented by the unusual type of beats alone, they correspond in outline to those obtained by stimulation of various areas of the ventricular musculature.†

Such extrasystoles are seen most commonly when the ventricular rate is relatively slow.

Now when digitalis is administered in large doses to patients who are suffering from complete irregularity of the heart, a bigeminal action of the ventricle is often observed when the retardation is marked. The pulse still presents irregularity, but it may happen that the shorter pauses of the bigeminy are of almost or quite constant length. This constancy of length is explained if we assume that the second or weaker beat of the bigeminy is a response to a ventricular impulse and is independent of auricular impulses.‡ An opportunity of putting the matter to the direct or galvanometric test has not occurred.§ The same type of irregular "bigeminy" is met with apart from digitalis administration, and an example of it is shown in Fig. 4 C.

CERTAIN CONDITIONS DIFFERENTIATED.

Cases in which the ventricular form of venous pulse occurs, but in which either auricular fibrillation is absent or in which the evidence is insufficient to justify us in assuming its presence.

The conclusion has been formed that of cases manifesting a ventricular form of venous pulse those which show complete irregularity of the heart belong to a single group, that of auricular fibrillation. It has also been

* It must be noted that abnormal ventricular variations may occur in beats arising as a result of auricular impulses— but the remaining arguments and observations prohibit such a supposition in this instance.

† Two types have been figured by Kraus and Nicolai** and have been allocated to right and left ventricle. But I may state as a result of observations as yet unpublished that no two points of stimulation give precisely the same picture, that a practically constant type is given from any single focus of stimulation, and that such type may be held within certain limits as characteristic of the focus or area in which it arises.

‡ The constancy of the short pause will receive the same explanation as that adopted in other cases of accurate coupling arising as a result of ventricular extrasystoles.

§ Electrocardiograms have since been obtained from two patients exhibiting the coupling in question. In each instance the second or smaller beat yielded an anomalous electric complex. The explanation of the coupling adopted in the text is therefore demonstrated as the correct one.

demonstrated that auricular inco-ordination may be present, and yet the pulse regular. But there are at least two types of case in which, while there is no venous sign of auricular contraction and the pulse is regular, auricular inco-ordination is certainly or probably absent. Such being the case, an opinion that auricular fibrillation exists is not justified, where the pulse is regular, in the absence of electrocardiographic records.

The first type is that in which the pulse rate is usually of normal or but slightly increased rate. The patients are not infrequently encountered, and offer signs of dilatation of the right heart with considerable distension of the veins. An example of a polygraph tracing is shown in Fig. 10.

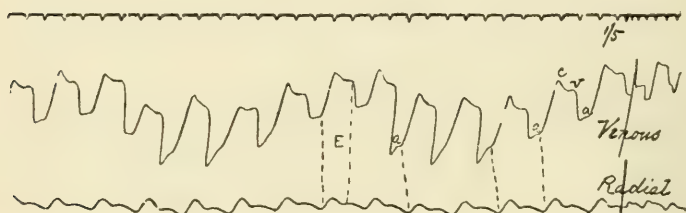


Fig. 10. The ventricular form of venous pulse in a patient with regular action of the heart. Auricular fibrillation was not present (CASE 14).

CASE 14.—F. W., a girl aged 12, had suffered from three attacks of rheumatic fever, and there was a clear history of pericarditis. The symptoms consisted of severe shortness of breath, cough and pain in the chest and upper abdomen. On examination the veins were seen to be greatly distended and the tension in them was increased. The pulse was regular and "water hammer" in character, capillary pulsation was present. The liver was enlarged and pulsatile, dropsy of the feet and ascites were found. The right limit of cardiac dulness was 2 inches and the left 6 inches from the mid sternal line. There was definite post-sternal dulness on a level with the second and third ribs. The lungs failed to cover the heart during deep inspiration and the heart's apex was fixed. An early diastolic murmur was audible over the greater part of the precordium, being maximal at the aortic cartilage. An occasional faint presystolic murmur and a constant systolic murmur were heard at the apex.

Aortic regurgitation, mitral stenosis and pleuro-pericardial adhesions, probably extending to the mediastinum, were diagnosed. The pulse was invariably regular, the jugular curves failed at almost all times to show any trace of presystolic elevation. In the tracing given (Fig. 10) a very faint trace of *a* wave is visible, but it was never more marked than here depicted, and usually could not be obtained. The electrocardiogram demonstrated a clear P variation (Fig. 25). The case is an example of the ventricular form of venous pulse accompanying the normal sequential chamber contraction. (Similar cases have been reported by Hering¹⁶ and Hewlett²¹.)

The second type of case is that of a not uncommon form of paroxysmal tachycardia.* I have met with three cases of a similar if not identical nature during the last six months. In one case mitral stenosis was found: in the other two no physical signs were apparent in the heart except during the paroxysms. The paroxysms were associated in the last two cases with slight but progressive dilatation, and the throbbing in the veins of the neck was sufficiently forcible to suggest arterial pulsation. Tracings are given from one of these patients in Fig. 11*a* and *b*. Fig. 11*a* was obtained between two paroxysms: Fig. 11*b* during a paroxysm. In the first curve the venous pulse is of the auricular and in the second of the ventricular form.

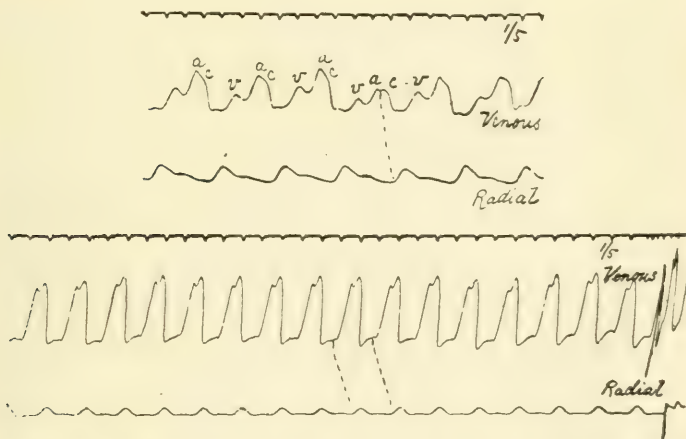


Fig. 11*a* and *b*. Two polygraph tracings from a patient with paroxysmal tachycardia. Tracing *a* is normal. Tracing *b* shows the venous pulse to be of the ventricular form while the paroxysm is in progress. The pulse is regular in both curves.

In both curves the arterial pulse is regular, the respective rates are 92 and 147. In the absence of electrocardiographic curves it is impossible to ascertain the nature of the mechanism. It may be of a kind suggested by Wenckebach⁶⁶, for it is possible that with an increased As-Vs interval the auricular contraction falls back on the preceding ventricular systole. In the case of mitral stenosis, previously referred to, this explanation would suffice, for a prolongation of the *a-c* and P-R intervals was present while the pulse

* Certain regular paroxysms accompanied by the ventricular form of venous pulse and described by Mackenzie⁶⁷ and Hewlett⁶⁸ may be included in this group.

was slow. In the patient from whom the figured tracings were taken no impairment of conductivity was ever noticed and the increase of rate was not great. We may perhaps be dealing with paroxysms starting in the ventricle.

The point of importance at present is the fact that interpretations other than auricular fibrillation suggest themselves, and that while the pulse is fast, but regular, the latter may be rationally excluded.

True "nodal rhythm" is a rare affection and gives rise to a clinical picture entirely at variance with that of the disorderly action of the heart hitherto considered.

In the preceding pages it has been demonstrated that the condition which has hitherto passed in this country under the name of "nodal rhythm" is in reality due to an inco-ordinate action of the auricle known to experimentalists as auricular fibrillation. In the discussion based on purely clinical data it was stated that it could be shown that auricle and ventricle are not contracting together. There are many reasons which militate against the acceptance of the view of synchronous contraction of the two chambers in complete irregularity of the heart. These reasons I do not propose to consider, for they will readily suggest themselves as a result of the observations which have been discussed. At the same time I desire to place on record, for purposes of contrast, a single and fully considered instance of what I regard as a case approaching as nearly as possible to what may be termed, in the present state of our knowledge, true nodal rhythm.* It will be shown that a rhythm may be generated in the auricle near to or at its junction with the ventricle, and that the clinical picture to which it gives rise is strikingly at variance with that which is presented by complete irregularity of the heart.

The following case is the only one of its kind which I have met with personally, and so far as I am aware only one patient showing signs of a similar though not identical nature has been so far recorded. The case referred to is that reported by Rühl⁵¹: the description of the case is meagre, but the venous curves show a condition of paroxysmal tachycardia and appear to substantiate the author's conclusion that during the paroxysms auricle and ventricle contracted simultaneously. The condition is therefore a very infrequent one.

The patient, a report of whose condition is now given, has been under continuous observation for many months, and, of the numerous observations which have been made upon him, attention will be chiefly directed to those which directly affect the general conclusions of the present communication.

* The term atrio-ventricular rhythm would perhaps be more consistent with our present knowledge: for while we may state with a fair degree of probability that such rhythms originate in the junctional tissues, their accurate location in the node is not possible at the present time.

CASE 15.—H. M., a labourer, aged 61, came to the out-patient department at the City of London Hospital on 4th October, 1909, complaining of pain in the left side of the chest, shortness of breath and palpitation.

Past illnesses.—As a child he contracted measles; twelve years ago he states that he had "blood poisoning" as a result of drain work, with fever, headache and vomiting. He was laid up for nine weeks. Five years ago he had rheumatic fever, but has not suffered from a return of this affection.

Present illness.—His symptoms date from March, 1909, when he was ill for three weeks with pain in the upper part of the stomach, loss of appetite, and vomiting. The vomit was white and contained slime; occasional clots of blood were ejected and the motions were black. The pain has continued in a less aggravated form but the vomiting has ceased. Discomfort in the epigastrium is experienced, amounting at times to actual pain of a lancinating character. The appetite is poor and the bowels are constipated. Shortness of breath has been present throughout, and is especially prominent upon moderate or severe exertion. He suffers from a sense of exhaustion, chiefly experienced in the legs. There is often a beating in the chest, more particularly when in the upright posture and after exercise. It has been absent at night, and is in abeyance while he is resting, but even when recumbent he has felt it at times. While standing he often becomes giddy and shaky in the limbs. He is losing weight.

Condition (4th October, 1909).—A poorly nourished, anæmic subject, who carries his years indifferently. There is general arterial disease: the arteries of the arms are conspicuous throughout the major part of their course. Systolic blood-pressure ranges from 110 to 150 mm. Hg. There are no signs of pleuro-pericardial adhesions or aneurism. The pulse is of the Corrigan type and capillary pulsation is present. The right limit of cardiac dulness is 1 inch and the left 4½ inches from the middle line. There is a systolic murmur at the apex beat, which is forcible, and the murmur is well conducted to the axilla and left scapula. The second sound is normal at the apex. At the aortic cartilage there is a faint but definite early diastolic murmur. There are no physical signs pointing to gross lesion of the stomach.

The chief feature of the case is an irregularity of the heart, which consists of occasional or frequent extrasystoles, and of short paroxysms of tachycardia. The interruptions of the otherwise regular rhythm are always present in some degree: they are usually frequent when the patient stands, but much less frequent while he is reclining. If examined in the standing posture the short paroxysms are always found, if laid on his back they promptly disappear, and for several hours the irregularities may be absent. But if at any time he stands again there is a return of the fleeting periods of tachycardia. Change of posture has been frequently ascertained to be almost invariable in its effects. The paroxysms do not occur in the sitting posture, and therefore cannot be ascribed to the action of gravity upon the heart. They are not present after or during exertion, or long periods of suspended respiration, in the recumbent posture. The postural observations have recently been extended by Dr. Marris of St. George's Hospital. He finds that there is a critical angle, during the change from horizontal to vertical lie, at which the ectopic beats appear. He has further observed that a tight abdominal binder abolishes the irregularity which prevails in the erect posture. Venous filling, or more properly the lack of it, therefore appears to be an important contributory factor in the production of the abnormal mechanism.

The reaction of the heart to posture has necessarily resulted in difficulty in obtaining venous curves. The paroxysmal venous curves have been won

on three occasions only. It has also rendered the simultaneous record of venous and electrocardiographic curves impossible: the electrocardiograms were taken with the patient standing. The paroxysms and single interruptions are immediately recognised by the patient when they occur.

The pulse, when regular between the paroxysms, is usually slow, its rate varies between 37* and 70 per minute. At times there is a certain degree of sinus arrhythmia. The extra or ectopic beats which interrupt the normal rhythm are of varied form, but most of them conform to the recognised pictures of auricular and "nodal" extrasystoles, when examined in the venous curves. The electrocardiographic tracings show at least four varieties, but as their nature is not entirely clear further reference to them will be postponed. More frequently than otherwise they differ from the beats of the paroxysm itself. In this respect they resemble the single interruptions met with in other cases of paroxysmal tachycardia.

The paroxysms consist of a series of regularly placed beats (there is some general diminution of rate as the individual attack proceeds), and the rate lies between 135 and 160 per minute. Alternation is very frequent, and in simultaneous electrocardiographic and radial curves the small beat in one may correspond to the large beat in the other, or vice versa. The onset of the tachycardia is marked by the occurrence of several anomalous beats which do not properly belong to it. In the radial curves (Figs. 27-28) they are differentiated by the low level which they occupy in the curve, and by their relative insignificance. Venous curves (Fig. 27, second paroxysm) may point to their having a higher origin† than the beats of the paroxysm proper. The high level of origin is also borne out by the electrocardiographic curves (Fig. 26), as will be seen later.

The contractions of the heart during the paroxysm proper yield venous curves which consist of high peaked waves, similar to those seen when auricle and ventricle are known to contract together (e.g., in complete heart-block and in cases of single ventricular extrasystole). The points at which *a* and *c* are estimated as due do not fall absolutely together, but they are nearer together than is the case with certain of the premonitory beats. The length of the interval is generally 0.06 sec., the *a-c* interval of the normal rhythm is 0.2 sec. (The presphygmie interval for normal and paroxysmal beats is the same on the arterial side). The venous curves definitely indicate that auricle and ventricle are in simultaneous contraction. Yet the auricular contraction commences at a slightly earlier time than does that of the ventricle. The interval is too short to permit of the conclusion that ventricle is responding to auricle, but, on the contrary, it may be supposed that the two chambers are contracting in response to a common source of impulse formation. It may be argued, from the evidence, that this common focus lies nearer to the auricle than to the ventricle. In other words, the

* This low rate occurred during sinus arrhythmia. The usual rate is 50-54.

† The higher the origin the greater is the *a-c* interval.

facts suggest that the impulses are derived from the neighbourhood of, or actually arise in, the node of Tawara (the junction of auricle and bundle).

The relationship of the auricular and ventricular systoles is borne out by the electrocardiographic curves. Comparing the beats of paroxysm and normal rhythm in Fig. 26, the essential difference between them lies in the shape of the variation which directly precedes R (the first event of the ventricular cycle); in the normal curve this variation P is recognised from its presystolic situation to be the result of auricular systole. In the paroxysmal beat a variation of similar extent is observed, but it is directed downwards instead of upwards. The complete inversion of P during the paroxysm very strongly suggests that the wave of contraction in the auricular walls has travelled in a direction the reverse of the normal. In previous communications I have already referred to the importance of these abnormal P waves, and to their significance as indicating an alteration of direction of beat and therefore a dislocation of the site of impulse formation upon which they are dependent. In the present instance it may be concluded that instead of passing from above downwards the wave of contraction has travelled from below upwards*. The interval P-R in the normal beat is 0.14 sec. and in the abnormal or paroxysmal beat it is 0.08 sec.. The difference between the two is less than would be anticipated from the venous curves, but both the nature of the abnormal P variation and the closing up of the P-R interval confirm the previous conclusion drawn from polygraph curves, namely, that the contraction of both auricle and ventricle is derived from a single impulse generated between auricle and ventricle, but rather nearer to the former than to the latter.

A fortunate experimental observation has placed both the measurements and the interpretation upon a satisfactory footing. In the figures so far discussed we have no simultaneous venous and electric curves, and the absence of such curves, curves which would have proved of value, is the necessary outcome of the postural changes of rhythm found in the patient. But the curves actually shown were taken within an hour of each other, and one may be read into the other. The experimental observation, to which we may now refer in detail is of particular value, not only because the electrocardiographic curves are identical with those already shown, but because in this instance we have simultaneous curves from auricle and ventricle, taken directly from the heart wall by means of myocardiographic levers. Fig. 29 consists of ventricular, auricular and electrocardiographic curves. It is an example of fibrillation of the auricle, and its offset and return to the normal rhythm (of which one beat, the last, is shown). The first part of the curve has been discussed in an earlier section. Attention is now directed to the last four beats (R^{13} and R^{14}). The portions of the ventricular

* In speaking of up and down, I use the terms in the morphological, and not necessarily in the anatomic, sense; for we are as yet unaware of the direction of the anatomic pathway of contraction in the auricle.

electrocardiographic curves are alike in the four instances, and consist of R and T variations. It is in the presystolic event that the notable variation occurs. Preceding the ventricular contractions R^{13} and R^{14} , the waves P (P^{20} and P^{21}) stand in marked contrast to the normal auricular variation (P^{23}) of the normal beat (R^{16}). They are completely inverted*. In the case of beat 15 a transition form is seen and scarce a trace of P remains (P^{22}). The explanation is to be sought in the accompanying myocardiograms. The As-Vs intervals are marked by the vertical lines and stand at 0.43, .043, .066, and .088 respectively. (The intervals have been measured and marked upon a greatly enlarged and photographic reproduction of the original curve.) (The commencement of the ventricular upstroke is not always as well defined as it might be, but the correctness of its position as marked may be readily checked by reference to the first notch of the plateau and to the peaks R.) The widening of the As-Vs interval occurs in two stages, and can be seen without measurement by glancing at the relative positions of the tops of the auricular myocardiographic curves and the bottoms of the ventricular myocardiographic curves. These simultaneous tracings demonstrate the mechanism of the heart beat corresponding to the electric curves in question in a conclusive manner. It is obvious that as an accompaniment of the decreased P-R interval (the figures stand at .065, .066, and .088), auricle and ventricle are in synchronous contraction, during portions of their respective cycles. For each auricular systole is of the same length whether it belongs to the normal or abnormal cycle. The same type of auricular electric curve and the presence of shortening of the P-R interval in the clinical example permits us to conclude that a similar mechanism is present, and confirms the previous deductions.

The intervals in the experimental curve are subject to several further considerations. In the first place there is a notable discrepancy between the shortening of the As-Vs intervals and the corresponding P-R intervals. The intervals for beat 16 are alike (namely, 0.88 sec.). The shortening of the As-Vs interval of beat 14 is to .043 sec., while that of the P-R interval is only to .065. The discrepancy, or difference in shortening, is approximately 0.02 sec.. Attention to this discrepancy is of interest, and it meets with a ready explanation, which is in accord with the remaining remarks. It is due to the position of the myocardiographic lever attached to the appendix of the auricle. If, as would be anticipated, the auricular appendix enters contraction before that portion of the auricular musculature which borders on the ring, a difference in the intervals would be expected. In the normal and abnormal beats considered, let it be allowed that the impulse travels downwards in the one case and upwards in the other, then a transmission

* Similar electrocardiograms (experimental) have been published by Hering, (*Archiv f. d. ges. Physiol.*, 1909, CXXVII, 155) but in the absence of myocardiographic curves their interpretation could not be undertaken with any degree of certainty. Experimental extrasystoles started at the inferior vena cava yield inverted P variations, but the extent of the dip is not so great as that which is presented by these curves.

time of .01 sec. for the single journey would suffice to explain the difference in the intervals. On one occasion I have obtained curves which bear out this explanation. Direct leads, with the electrodes of Gotch²⁷, were instituted from the base of the superior vena cava and from the upper end of the inferior vena cava, while the auricle was in fibrillation. Suddenly the fibrillation ceased spontaneously and was succeeded by several beats of the heart as a whole, in which the mechanism was abnormal, before the final normal rhythm and sequence were established. The normal beats of the re-established rhythm were accompanied by auricular contractions which yielded electric variations of constant excursion and direction, the main variation showing electro-negativity of the upper lead with a lesser swing in the positive direction following it. The abnormal beats on the other hand, in which the P-R interval was reduced, showed the reverse picture, the excursions remained the same but the direction altered from negative to positive and positive to negative respectively. In the case of the normal beat we have to assume primary* activity of the tissues abutting on the superior vena cava; in the case of the abnormal beat on the contrary we have equally to assume primary activity in the tissues in the neighbourhood of the inferior vena cava. All the evidence leads us to conclude therefore, that at times the contraction wave is temporarily reversed in the auricle when the latter breaks back from fibrillation to the normal response to the heart's pace-maker†.

Now a similar discrepancy has been noted in the clinical instance between the *a-c* and P-R intervals, but a like explanation will not apply. It is probably attributable to the abnormality of the contraction in the instance of the reversed beat, and to a later appearance of *a* in the veins of the neck under these conditions. The comparison is of chief importance in emphasising the greater accuracy of the P-R as opposed to the *a-c* interval in the clinical instance. The *a-c* interval during the paroxysm is not an absolutely true representation of the As-Vs interval, it is too short, and the electric measurement, .08 sec., is the more accurate.

The parallel between clinical and experimental curves is striking, but if further evidence were required, it would be found in the relative heights of the peaks R in the two instances. The peaks R which follow inverted P variations are always higher, whether they are observed in the clinical or experimental example.

The experimental curves show us conclusively that we are dealing with simultaneous auricular and ventricular contraction. That there is only a small reduction of the normal As-Vs interval is immaterial from this point of view, but it is of importance in demonstrating that the level

* Referring to superior and inferior vena cava only.

† Winterberg²⁸ has made certain observations which tend to the same conclusion. The auricular impulses, at the escape from fibrillation, are not necessarily generated in the "sinus," they may arise in other portions of the auricular walls.

of impulse formation is relatively high so far as the ventricle is concerned. The main delay is in the bundle itself.*

The close analogy between the two sets of curves allows of similar conclusions in the clinical instance. The difference in the P-R intervals of normal and abnormal beats in the patient is greater than in the experiment. But the auricle of man is larger than that of the dog. The normal P-R interval in the patient is nearly twice that found in the animal.

Returning again to the clinical case, in Fig. 28 it will be seen that there is irregularity during the paroxysm itself, and that this irregularity is due to the presence of premature beats interrupting an otherwise regular rhythm. One of the interrupting beats has been caught electrocardiographically and is shown in Fig. 30. The extra beat is of the type recognised as due to an extrasystole of the left ventricle. Now the pause which follows the premature beat is fully compensatory, and this in itself is valuable confirmatory evidence of the auricular origin of the ectopic rhythm which it disturbs. The supraventricular origin of the paroxysmal beat is also shown by the shape of the ventricular electric complex.

Another point of interest in the clinical curves is well seen in the first escaped beat of Fig. 26. Here neither normal nor inverted P variation is present. Such heart cycles have been of common occurrence in this patient at the termination of paroxysms, and many such beats interrupt the normal rhythm. A complete parallel is found in beat 15 of Fig. 29. One may infer from an examination of the intervals, if not from *a priori* arguments based on the isoelectric interval directly preceding the peak R¹⁵, that this is an example of a transition form between beats 14 and 16. That is to say, that we are dealing with a beat which starts at a higher level than beat 14, and at a lower level than beat 16. In brief, it has its origin at a point lying between the normal pace-maker† and the lowest or junctional level of the auricular tissue. The same conclusion applies to clinical beats of a similar nature seen in Fig. 26. Of the escaped beats in Fig. 26, the first and second probably belong to this category, while the third is of the same nature as the beats of the paroxysm.

* That auricle is not giving the pace to the ventricle is certain, for the following reasons:—An increased conductivity would not be expected during the clinical paroxysm, for the rate is increased. Neither would a gradually decreasing conductivity be anticipated in the escaped beats following the fibrillation, for the rate is lowered and blocking of some of the fibrillary impulses was previously present.

† For the purposes of the argument there is no need to place the normal pace maker of the heart in the neighbourhood of the superior vena cava, but as a matter of fact the evidence as a whole points in this direction. In a single experiment, using direct leads from various parts of a dog's auricle, it was found that the neighbourhood of the superior vena cava becomes electronegative or active before either appendix, inferior vena cava or a point of musculature at the groove directly below the superior vena cava on the front of the heart. In several experiments it was found that the auricular electric complex of extrasystoles induced in different parts of the auricle shows notable variations. The auricular complex of extrasystoles originating near the superior vena cava resembles the normal complex most closely. This evidence points very definitely to the presence of the pace-maker in the neighbourhood of the superior cava.

The conclusion that in the clinical case paroxysms are present, and that each paroxysm consists of a rhythm created by impulses which are derived from the lower levels of the auricular tissue, or, in other words, in the neighbourhood of the node, depends upon the evidence which has been given and which may be briefly summarised as follows*:—1) Upon the shortened *a-c* and P-R intervals. The extent of the shortening and the circumstances under which it occurs (pulse rate, etc.) preclude the possibility that ventricle responds to auricle.

2) Upon the complete reversal of the electrical variation accompanying the auricular contraction.

3) Upon the presence of a normal type of ventricular electric complex, and the occurrence of the complete compensatory pause following the interruption of the ectopic rhythm by a ventricular extrasystole. These facts indicate the supraventricular nature of the rhythm.

4) Upon a close comparison with duplicate curves obtained experimentally, and upon the more accurate analysis which could be undertaken in the latter.

It is a matter of importance that it should be recognised that such a phenomenon as "nodal rhythm," in the broad sense of the word, does exist in clinical medicine: it is also imperative that its rarity should be acknowledged. And further, and most important, it must be understood that the picture presented by the only cases exhibiting it, of which we have knowledge, is entirely at variance with that of the condition which has hitherto passed under this term. "Nodal rhythm," as we now know it, is a rhythm in which there are definite signs of simultaneous auricular and ventricular contraction: *a fortiori* the rhythm is regular. It falls into line with the examples of fast and paroxysmal ectopic rhythms, arising at different levels: in these also the individual beats can be shown to spring from a single and fixed focus. It may be taken as a general rule that a paroxysmal rhythm, when regular, arises as a result of impulses generated in a single focus. The converse, that irregular paroxysms are generated from several foci, only applies if such paroxysms are fast, and if irregularities resulting from conductivity and contractility changes can be excluded.

In conclusion it is my pleasant duty to acknowledge my gratitude to those who have brought material for observation to my notice, and to those who have facilitated the examination of such material. I am indebted to all the members of the medical staff, honorary and resident, at University

* Before leaving this patient several points must be referred to which are in harmony with observations upon other cases of ectopic paroxysm, and they have been utilised in the discussion upon the subject in a paper published in the last number of this *Journal*. In the first place there is the presence of the premonitory contractions at the commencement of the paroxysms, and these are of a different nature to those obtaining in the paroxysm itself. Secondly, there is the fact that the beats which disturb the heart's regular action between the paroxysms are as a rule of a different form to those of the paroxysm. Thirdly, there is the marked depression of rate with subsequent acceleration at the cessation of the paroxysm (clearly seen in Fig. 28).

College Hospital. My thanks are especially due to Dr. James Mackenzie and to Dr. John Rose Bradford.

CHIEF CONCLUSIONS.

1. Amongst the many forms of persistent irregularity of the human heart, none is more common than that which may be termed complete irregularity of the heart. It is accompanied by an absence of all sign of normal auricular action; and it is due to fibrillation of the auricle.

2. Auricular fibrillation as a pathological and clinical entity exhibits certain definite signs. Amongst the distinguishing features the following are the most important.

a) Absolute irregularity of the ventricle.

b) The ventricular form of venous pulse.

c) A characteristic electrocardiogram, in which the ventricular curve is of the usual type, but in which the normal auricular representative is replaced by a series of rapid oscillations, which are superimposed upon the rest of the curve and deform it. The oscillations are generated in the auricle, and are the result of the fibrillation.

3. Digitalis retards the ventricular rate in clinical auricular fibrillation by enhancing a previously existing auriculo-ventricular heart-block. The rapid and irregular impulses showered upon the ventricle from the fibrillating auricle are hindered in their passage from one chamber to the other by the action of drugs of this class. The influence of digitalis is exerted, directly or through the vagus, upon the junctional tissues.

4. Auricular fibrillation in man may be accompanied by heart-block of all grades, and the heart-block may or may not result from digitalis administration. When the heart-block is complete the ventricular action is slow and regular.

5. A rhythm arising in the neighbourhood of the node of Tawara is a real clinical phenomenon. It is distinct from the mechanism which produces complete irregularity, and it is a rare affection.

BIBLIOGRAPHY.

- ¹ BAMBERGER (H.). *Lehrbuch der Krankheiten des Herzens*. Wien, 1857, s. 100.
- ² BROADBENT (W.). *The Pulse*. London, 1890.
- ³ CUSHNY (A. R.) and EDMUNDS (C. W.). Paroxysmal irregularity of the heart and auricular fibrillation. *Studies in Pathology, etc.* (ed. by Bulloch), Aberdeen, 1906.
- ⁴ CUSHNY (A. R.) and EDMUNDS (C. W.). Paroxysmal irregularity of the heart and auricular fibrillation. *Amer. Journ. of Med. Sci.*, 1907, cxxxiii, 66-77 (the paper is practically a reprint of the former one).
- DE VRIES (H.). *Arrhythmia Perpetua*. Groningen, 1908 (proof sheet).
- ⁵ EINTHOVEN (W.). Le télécardiogramme. *Archiv. Internat. d. Physiol.*, 1906, iv, 132-164.
- ⁷ EINTHOVEN (W.). Weiteres über das Elektrokardiogramm. *Archiv f. d. ges. Physiol.*, 1908, cxvii, 517-584.
- ⁸ FAGGE (H.). On the murmurs attendant upon mitral contraction. *Guy's Hosp. Rep.*, 1871, xvi, 247-342.
- ⁹ FREDERICQ (L.). Rythme affolé des ventricules dû à la fibrillation des oreillettes. *Physiologie du faisceau auriculo-ventriculaire*. *Archiv. Internat. d. Physiol.*, 1904-5, ii, 281-285.
- ¹⁰ GIBSON (A. G.). The significance of a hitherto undescribed wave in the jugular pulse. *Lancet*, 1907, ii, 1380-1382.
- ¹¹ GIBSON (G. A.). A discussion on some aspects of heart-block, IV. *Brit. Med. Journ.*, 1906, ii, 1113-1119.
- ¹² GOTCH (F.). Capillary electrometer records of the electrical changes during the natural beat of the frog's heart. *Proc. Roy. Soc., B.*, 1907, lxxix, 323-328.
- ¹³ GOTCH (F.). The succession of events in the contracting ventricle as shown by electrometer records (tortoise and rabbit). *Heart*, 1910, i, 235-261.
- ¹⁴ HERING (H. E.). Zur experimentelle Analyse der Unregelmässigkeiten des Herzschlages. *Archiv f. d. ges. Physiol.*, 1900, lxxxii, 1-33.
- ¹⁵ HERING (H. E.). Analyse des Pulsus irregularis perpetuus. *Prag. med. Wochenschr.*, 1903, xxviii, 377-381.
- ¹⁶ HERING (H. E.). Ueber die häufige Kombination von Kammervenenpuls mit Pulsus irregularis perpetuus. *Deutsch. med. Wochenschr.*, 1906, xxxii, 213-215.
- ¹⁷ HERING (H. E.). Über den Pulsus irregularis perpetuus. *Deutsch. Archiv f. klin. Med.*, 1908, xciv, 185-204.
- ¹⁸ HERING (H. E.). Das Elektrokardiogramm des Irregularis perpetuus. *Deutsch. Archiv f. klin. Med.*, 1908, xciv, 205-208.
- ¹⁹ HERING (H. E.). Über das Elektro-Kardiogramm (mit Demonstration von Projektionsbildern). *Verhandl. d. Kongress. f. inn. Med.*, Wiesbaden, 1909, xxvi, 612-3.
- ²⁰ HERING (H. E.). Ueber das Fehlen der Vorkofzacke (P) im Elektrokardiogramm beim Irregularis perpetuus. *Münch. med. Wochenschr.*, 1909, lvii, 2483-85.
- ²¹ HEWLETT (A. W.). The interpretation of the positive venous pulse. *Journ. of Med. Research*, 1907, xvii, 119-136.
- ²² HEWLETT (A. W.). Clinical observations on absolutely irregular hearts. *Journ. Amer. Med. Assoc.*, 1908, li, 655-659.

- ²⁰ HIRSCHFELDER (A. D.). Some variations in the form of the venous pulse. *Johns Hopkins Hosp. Bull.*, 1907, XVIII, 265-267.
- ²¹ HIRSCHFELDER (A. D.). Contributions to the study of auricular fibrillation, paroxysmal tachycardia, and the so-called auriculo-(atrio-) ventricular extrasystole. *Johns Hopkins Hosp. Bull.*, 1908, XIX, 322-326.
- ²² JANOWSKI (W.). Über die diagnostische und prognostische Bedeutung der exakten Pulsuntersuchung. *Samml. klin. Vorträge (Volkmann)*, 1897, N.F., Nr. 192-3 (Inn. Med., 57), 975-1056.
- ²³ KRAUS (F.) and NICOLAI (G. F.). Ueber das Elektrokardiogramm unter normalen und pathologischen Verhältnissen. *Berlin. klin. Wochenschr.*, 1907, XLIV, 765-768; and 811-818.
- ²⁴ KRAUS (F.) and NICOLAI (G.). Ueber die funktionelle Solidarität der beiden Herzhälften. *Deutsch. med. Wochenschr.*, 1908, XXXIV, 1.
- ²⁵ KRONECKER (H.) and SPALLITTA (F.). La conduction de l'inhibition a travers le cœur du chien. *Archiv. Internat. d. Physiol.*, 1904-5, II, 223-228.
- ²⁶ LEWIS (Th.). Irregular action of the heart in mitral stenosis; the inception of the ventricular rhythm, etc.. *Quart. Journ. of Med.*, 1908-9, II, 356-367.
- ²⁷ LEWIS (Th.). a) Paroxysmal tachycardia. *Heart*, 1909, I, 43-72.
b) The experimental production of paroxysmal tachycardia and the effects of ligation of the coronary arteries. *Heart*, 1909, I, 98-137.
- ²⁸ LEWIS (Th.). Auricular fibrillation; a common clinical condition. *Brit. Med. Journ.*, 1909, II, 1528.
- ²⁹ LEWIS (Th.). *Trans. Med. Soc. London*, 13-12-09. "Auricular Fibrillation," *Lancet*, 1909, II, 1820.
- ³⁰ LEWIS (Th.). Paroxysmal tachycardia, the result of ectopic impulse formation. *Heart*, 1910, I, 262-282.
- ³¹ MACKENZIE (J.). *The Study of the Pulse, etc.*. Edinb. and London, 1902.
- ³² MACKENZIE (J.). The inception of the rhythm of the heart by the ventricle, as the cause of continuous irregularity of the heart. *Brit. Med. Journ.*, 1904, I, 529-536.
- ³³ MACKENZIE (J.). New methods of studying affections of the heart. *Brit. Med. Journ.*, 1905.
a) I.—Affections of the function of conductivity, 1905, I, 519-522.
b) II.—The action of digitalis on the human heart, 1905, I, 587-589.
c) III.—The action of digitalis on the human heart—(*continued*), 1905, I, 702-705.
d) IV.—Action of digitalis on the human heart in cases where the inception of the rhythm of the heart is due to the ventricle, 1905, I, 759-762.
e) V.—The inception of the rhythm of the heart by the ventricle, 1905, I, 812-815.
- ³⁴ MACKENZIE (J.). The interpretation of the pulsations in the jugular veins. *Amer. Journ. Med. Sci.*, 1907, CXXXIV, 12-34.
- ³⁵ MACKENZIE (J.). Abnormal inception of the cardiac rhythm. *Quart. Journ. of Med.*, 1907-8, I, 39-48.
- ³⁶ MACKENZIE (J.). *Diseases of the Heart*, London, 1908.
- ³⁷ MACKENZIE (J.). Nodal bradycardia. *Heart*, 1909, I, 23-42.
- ³⁸ McWILLIAM (J. A.). On the phenomena of inhibition in the mammalian heart. *Journ. of Physiol.*, 1888, IX, 345-395.
- ³⁹ MAGNUS-ALSLEBEN (E.). Zur Kenntnis der Arythmia perpetua. *Deutsch. Archiv f. klin. Med.*, 1909, XCVI, 346-355.

- ⁴⁰ MAHOMED (F. A.). *Medical Times and Gazette*, 1872, I, 427.
- ⁴¹ MAREY (E. J.). *Physiologie médicale de la Circulation du Sang*, etc., Paris, 1863.
- ⁴² MINKOWSKI (O.). Die Registrierung der Herzbewegung am linken Vorhof. *Deutsch. med. Wochenschr.*, 1906, XXXII, 1248-1250.
- ⁴³ MORROW (W. S.). The various forms of the negative or physiological venous pulse. *Brit. Med. Journ.*, 1906, II, 1807-1812.
- ⁴⁴ MÜLLER (G.). Ungewöhnliche Dilation des Herzens und Ausfall der Vorhofsfuction. *Zeitschr. f. klin. Med.*, 1905, LVI, 520-528.
- ⁴⁵ PHILLIPS (F.). Sur les trémulations fibrillaires du cœur du chien. *Acad. roy. de Belg., Bull. d. l. Classe d. Sc.*, 1903, 455-469 (Fig. 4).
- ⁴⁶ PHILLIPS (F.). Les trémulations fibrillaires des oreillettes et des ventricules du cœur de chien. *Archiv. Internat. d. Physiol.*, 1904-5, II, 271-280.
- ⁴⁷ RADASEWSKY (M.). Über die Muskelerkrankungen der Vorhöfe des Herzens. *Zeitschr. f. klin. Med.*, 1895, XXVII, 381-410.
- ⁴⁸ RAUTENBERG (E.). Die Registrierung der Vorhofpulsation von der Speiseröhre aus. *Deutsch. Archiv f. klin. Med.*, 1907, XCI, 251-290.
- ⁴⁹ RAUTENBERG (E.). Ueber Synergie und Asynergie der Vorhöfe des menschlichen Herzens. *Münch. med. Wochenschr.*, 1909, LVI, 378-384.
- ⁵⁰ RIEGEL (Fr.). a) Ueber den normalen und pathologischen Venenpuls. *Deutsch. Archiv f. klin. Med.*, 1882, XXXI, 1-62.
b) Ueber Arrhythmie des Herzens. *Samml. klin. Vorträge (Volkmann)*, 1898, N.F., Nr. 227 (Inn. Med., Nr. 68), 1309-1338.
- ⁵¹ RIHL (J.). Ueber atrioventriculäre Tachycardie beim Menschen. *Deutsch. med. Wochenschr.*, 1907, XXXIII, 632-634.
- ⁵² RIHL (J.). Ueber das Verhalten des Venenpulses unter normalen und pathologischen Bedingungen. *Zeitschr. f. exper. Pathol. u. Therap.*, 1909, VI, 619-688 (Fig. 5, 12, 25, and 33a).
- ⁵³ ROTHBERGER (C.) and WINTERBERG (A.). Vorhofflimmern und Arrhythmia perpetua. *Wien. klin. Wochenschr.*, 1909, XXII, 839-844.
- ⁵⁴ SANSOM (A. E.). *The Diagnosis of Diseases of the Heart*, etc., London, 1892.
- ⁵⁵ SCHÖNBERG (S.). Über Veränderungen im Sinusgebiet des Herzens bei chronischer Arrhythmie. *Frankfurter Zeitschr. f. Pathol.*, 1908, II, 153-179.
- ⁵⁶ SKODA (J.). *Abhandlung über Perkussion und Auskultation* (vierte Aufl.), Wien, 1850, s. 313.
- ⁵⁷ SOMMERBRODT (J.). Ueber Allerhythmie und Arrhythmie des Herzens und deren Ursachen. *Deutsch. Archiv f. klin. Med.*, 1877, XIX, 392-423.
- ⁵⁸ STEELL (G.). *The Use of the Sphygmograph in Clinical Medicine*, Manchester, 1899.
- ⁵⁹ THEOPOLD (J.). Ein Beitrag zur Lehre von der Arrhythmia Perpetua. *Inaug. Dissert.*, Naumberg, 1907.
- ⁶⁰ WALSH (W. H.). *A practical Treatise on the Diseases of the Heart*, etc. (4th edit.), London, 1873, Plate I, Fig. 8, 10 and 11.
- ⁶¹ WENCKEBACH (K. F.). Beiträge zur Kenntnis der menschlichen Herztätigkeit. *Archiv f. Anat. u. Physiol., Phys. Abth.*, 1906, 297-354.
- ⁶² WENCKEBACH (K. F.). Beiträge zur Kenntnis der menschlichen Herztätigkeit. *Zweiter Teil*. *Archiv f. Anat. u. Physiol., Phys. Abth.*, 1907, 1-24.
- ⁶³ WENCKEBACH (K. F.). Beiträge zur Kenntnis der menschlichen Herztätigkeit. *Dritter Teil*. *Archiv f. Anat. u. Physiol., Phys. Abth.*, 1908, Suppl., 53-86.

- ⁸⁷ WINTERBERG (H.). Studien über Herzflimmern. III. Mitteilung. A. Über das Wesen der postundulatorischen Pause. B. Über den Einfluss des Flimmerns auf die Kontraktilität des Herzmuskels. *Archiv f. d. ges. Physiol.*, 1909, cxxviii, 471-518.
- ⁸⁸ YOUNG (C. L.) and HEWLETT (A. W.). The normal pulsations within the oesophagus. *Journ. of Med. Research*, 1907, xvi, 427-434.

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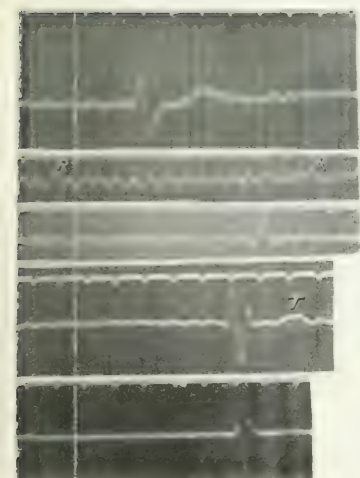
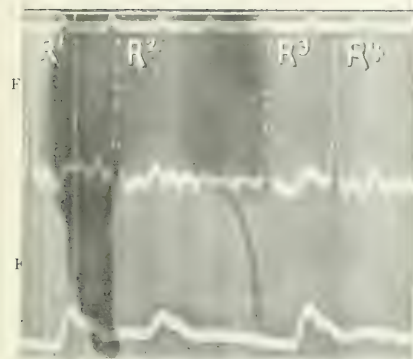
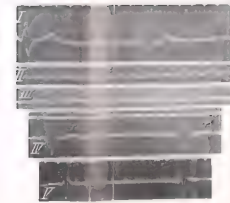
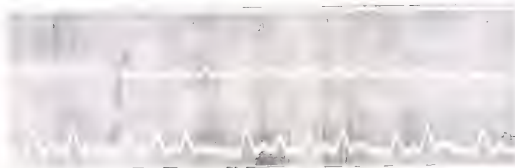
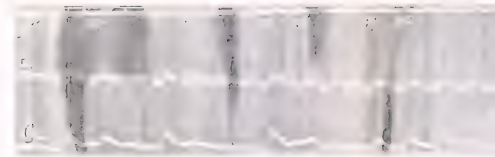
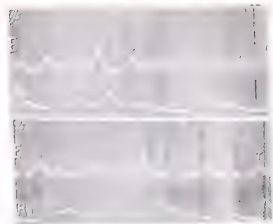
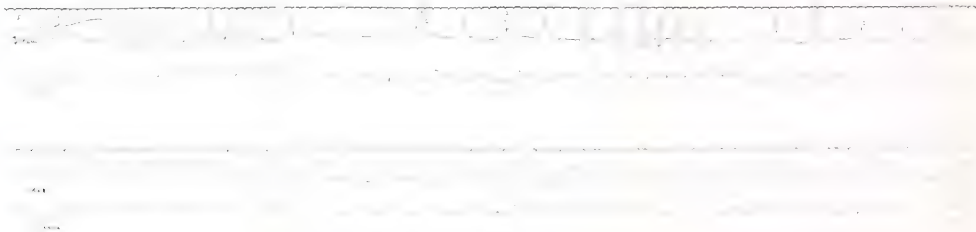
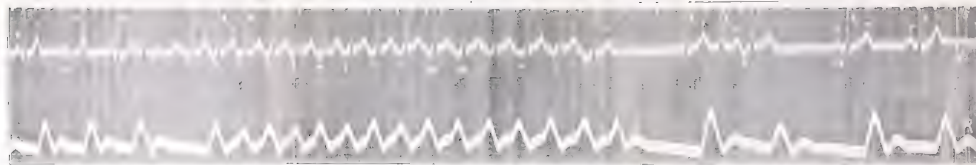


Fig. 18.







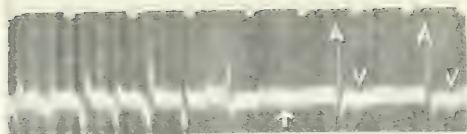


Fig. 31. A series of experimental

CURVE I.

Leads from a point inferior vena cava. The point the coordinate variations.



CURVE II.

A similar curve. The curves the oscillations and

CURVE III.

Leads from two points one below and near the oscillations are seen. Up and a slight escape of



CURVE IV.

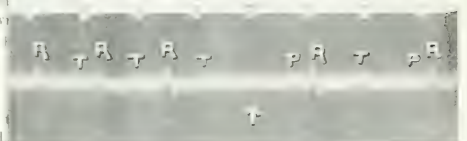
From the same point last curve shows that the fibrillation and auricular

Curves III and IV show of the separate auricular oscillations are R during fibrillation, for variations is greater in I



CURVE V.

Leads from the upper centre and whole length neck, the lower one upon translation was included the oscillations are shown. Up to this constant point.



CURVE VI.

The same leads as approximately threefold extent. The ventricular curves to be of essentially the

The electrode site

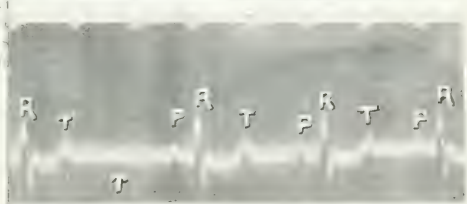
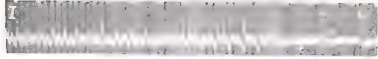


Fig. 31



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